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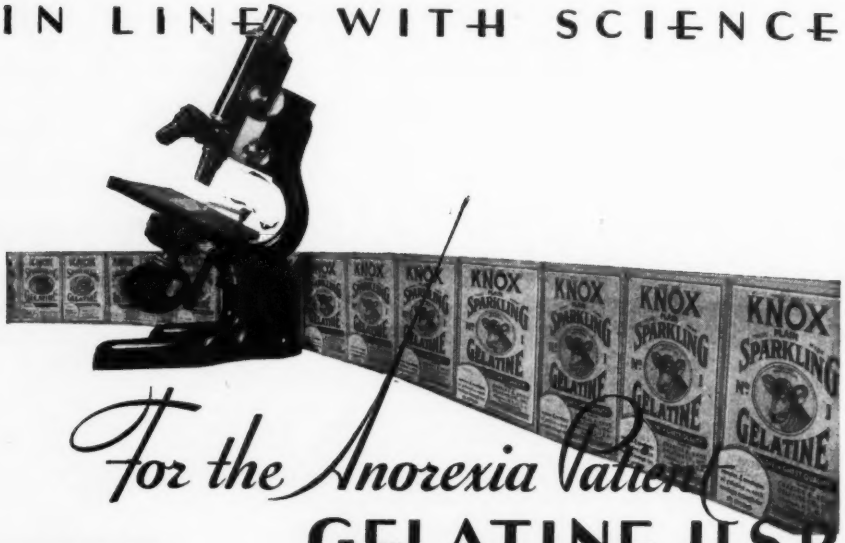

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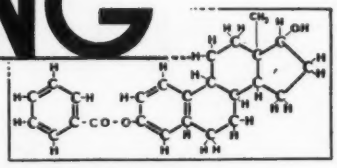

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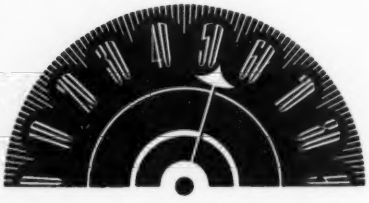

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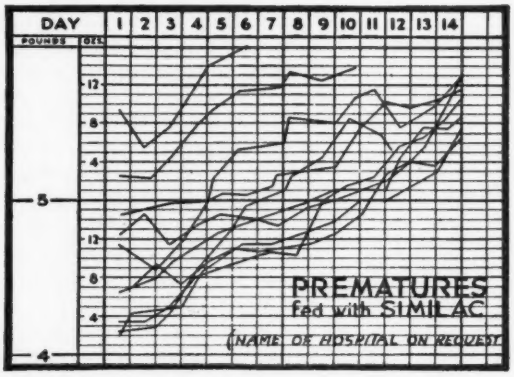

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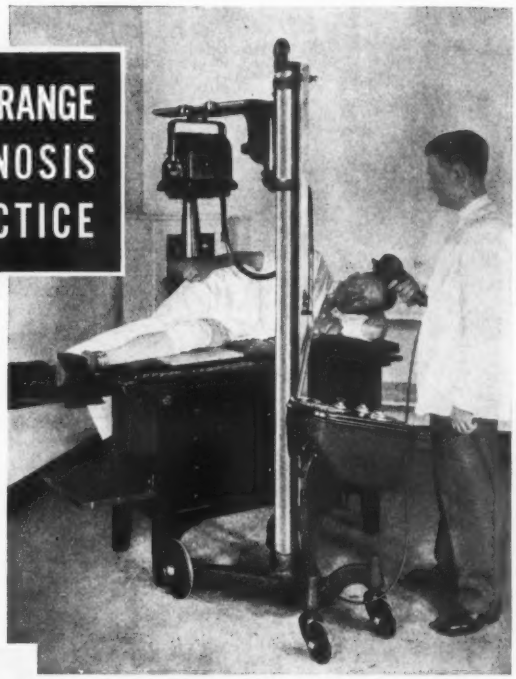

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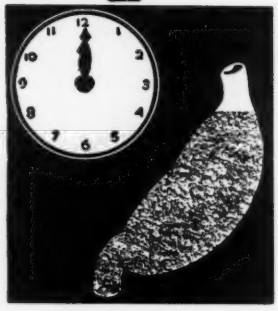

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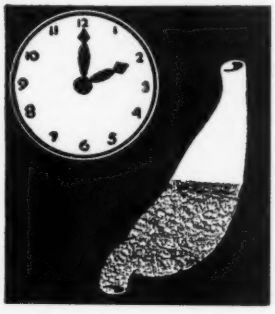

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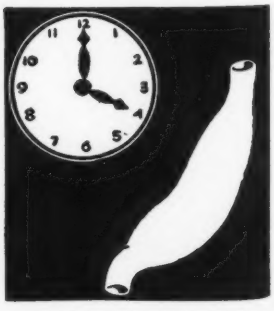

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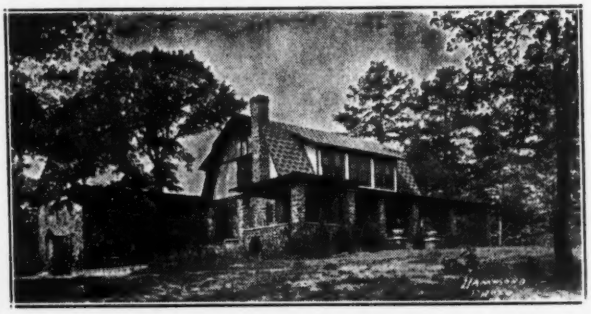

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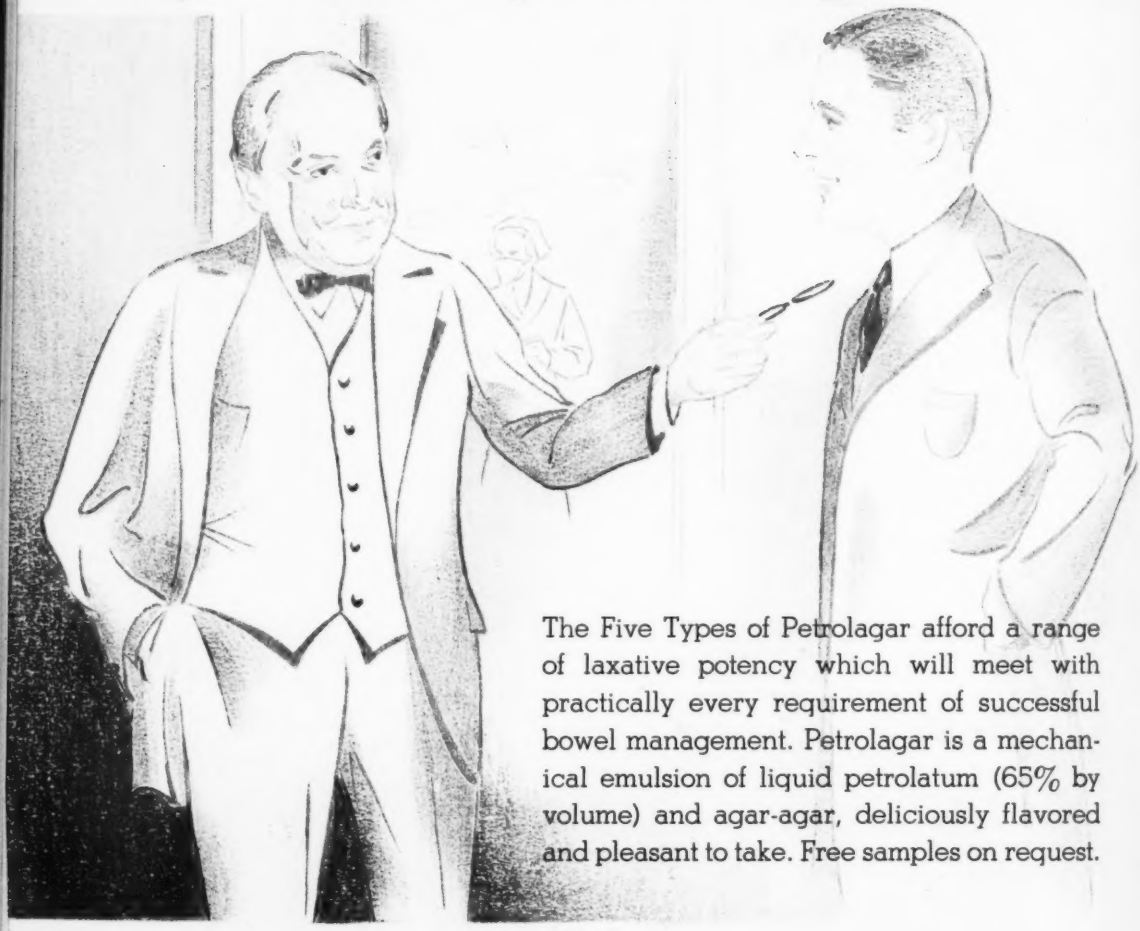

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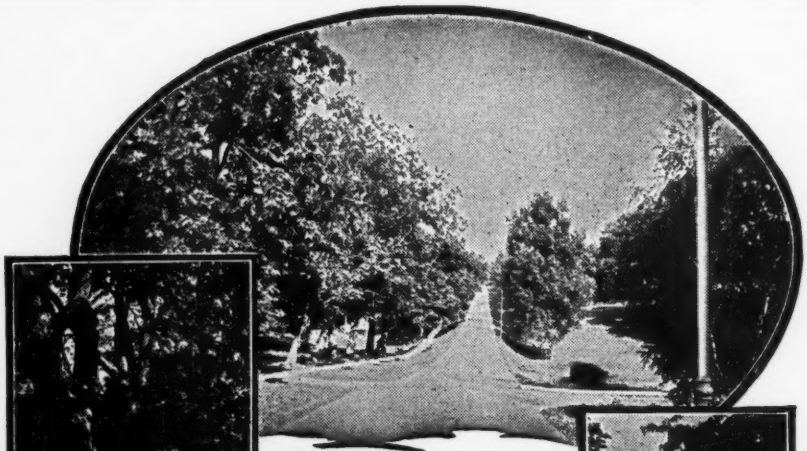

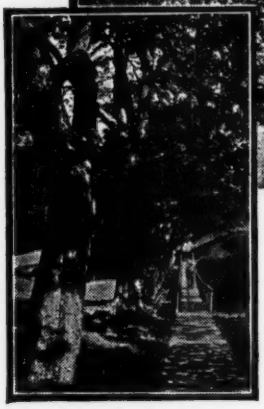

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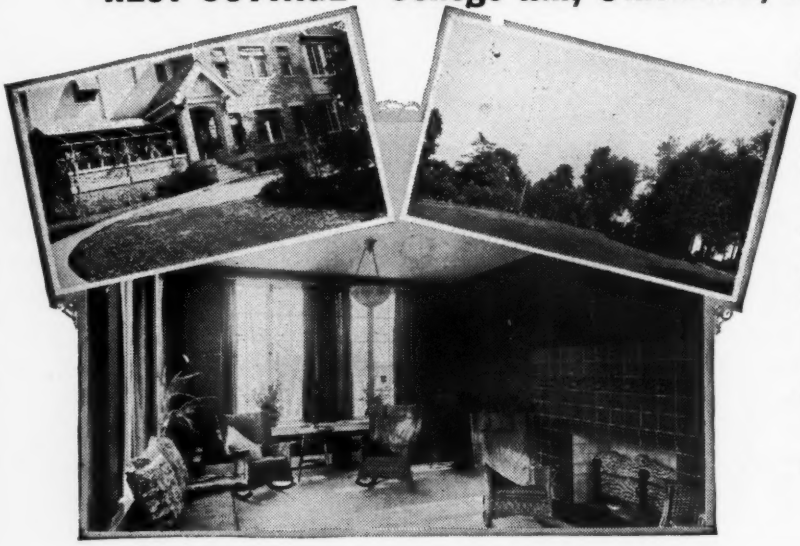

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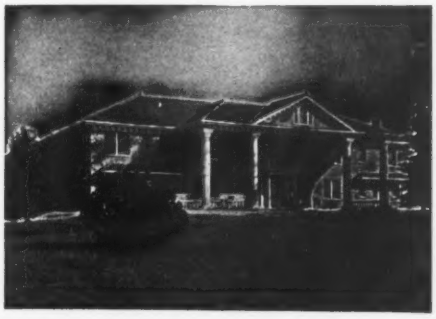

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Volume 29 MARCH 1936 Number 3

RADIATION THERAPY IN CANCER OF THE MOUTH, PHARYNX AND LARYNX*

By J. M. MARTIN, M.D., F.A.C.R.,
Dallas, Texas

Only a few years ago cancer of the mouth and throat usually meant an early and terrible death. Even with our present knowledge of the subject, greatly improved technic and equipment, cancer in these areas is still a serious disease and each case must be treated as an individual entity. But one hard and fast rule can be applied to all cases alike, namely: the diagnosis must be made early and the treatment must be efficient. If this rule could be universally adopted and rigidly enforced in every case, the present high death rate from cancer of the mouth, pharynx and larynx would be materially reduced.

Some of our preconceived ideas about cancer in and about the mouth have undergone radical changes in the past ten years. In the days when cancer of the lip, alveolar areas, tongue, pillars, tonsils and adjoining regions was wholly in the hands of the surgeon, a block dissection of the superficial lymph nodes beneath the mandible and along the lymphatic chains of the neck was thought to be necessary in practically every case. While cancer in the mouth is prone to metastasize earlier than cancer of the lower lip, experience has proven that metastases do not take place as early as we formerly believed. Even in the hands of an experienced and well trained surgeon, an extensive block dissection of the lymph nodes of the neck is followed by a mortality which must not be ignored. In early cases of carcinoma in the areas under consideration, palpable nodes may be, and often are, due to inflammatory processes that will rapidly clear up with improvement of the primary lesion. It is, therefore, our opinion that in early cases of cancer of the lower lip and mouth without demonstrable extension to the lymph nodes, routine block dissection is not indicated. Since a relatively small per cent metastasize early, all cases should not be subjected to a dangerous and mutilating operation unless there are justifiable indications.

Radiation equipment and technic, in the treatment of carcinoma, have advanced to a stage where curative results compare favorably with surgery. Some of the advantages in favor of radiation are: a negative mortality, a minimum degree of discomfort, hospitalization only in advanced cases and little or no scar or deformity.

The successful treatment of carcinoma includes a careful consideration of the general health of the patient. This is particularly true in elderly people and in the late stages of the disease. While some methods of cancer therapy are of greater curative value than others, no one remedy can be universally used to the exclusion of all others. The type, stage and location of a growth may require one or a combination of methods to effect temporary relief or a permanent cure. During and after radiation treatment of carcinoma wherever located, the care and comfort of the patient is sometimes as important as the treatment of the lesion. This is particularly true in cases of carcinoma of the mouth, pharynx and larynx. The problem of mouth washes, soothing lotions and sprays for the removal of secretions from the mouth and air passages are problems of no small importance. The diet and the methods of feeding these patients will often tax the ability of both physician and nurse to the limit. In advanced cases the success of any method of treatment will depend upon supportive measures, of which good food in sufficient quantities, iron, liver and glucose therapy are most important.

While this paper deals mainly with radiation therapy, it must not be understood that we are antagonistic to surgical methods when and where

*Read in Section on Radiology, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

*From Baylor University Hospital.

indicated. However, it is our feeling that in the regions under consideration, pure surgery should play a secondary roll. It is now about thirty-nine years since x-rays were discovered and about thirty-four years since their therapeutic value in the treatment of carcinoma was demonstrated. Still, today, probably not more than 50 per cent of all cancer cases subjected to radiation are properly treated.

Dr. Pusey's early work with x-rays in the treatment of skin cancer was remarkably successful. A review of his articles in the *Journal of the American Medical Association*[1 2 3 4 5 6 7] from 1901-5 would be enlightening to many of the younger men now engaged in radiation therapy. He had a remarkable understanding of the effects of radiation and a confidence in the method that enabled him to carry results to a successful issue in many cases of cancer of the skin. From clinical experience he developed a technic not unlike the Coutard method of today.

For more than twenty-five years, the author's[8] x-ray technic in the treatment of superficial carcinoma has changed but little. In the beginning, the voltage and amperage were low, and the rays were unfiltered. Exposures lasting ten to fifteen minutes were given every day or every other day until a distinct dermatitis was produced in the skin over the lesion. In cases that did not respond promptly, a second series of exposures was given. Surprisingly good results were obtained in most cases. Later, filtration was added; the voltage, amperage and target skin distance were increased, and the exposures were given every forty-eight hours until a distinct reaction in the tissues was produced. This technic,[9] somewhat refined, is in regular use in our laboratory today.

CANCER OF THE LIP

Radiation therapy in the treatment of carcinoma of the lip is now universally considered the method of choice because of the superior cosmetic results obtained. The age, size and extent of the growth will, in most cases, determine the method to be employed. Before the advent of properly filtered radium needles all cases of carcinoma of the lower lip were treated with x-rays with satisfactory results except in cases where the inside of the mouth was involved. It seems best at this time to confine our superficial x-ray technic to carcinomas of the lip that range in size up to a little more than an inch in diameter. An area a little larger than the growth is exposed on alternate days. Four, six, and sometimes twelve doses, depending upon the size of the tumor, are administered. A severe reaction follows this method of treatment, but resolution is complete in from six weeks to two months, and the lack of scarring, deformity and other unpleasant after effects is evident, as shown in cases illustrated in *Figs. 1* and *2*. When the tumors are large, involving the greater part or all of the lower lip and extend into the cheek at the corner of the mouth, or when they are deeply indurated, the weak radium needle technic described under the heading of oral cancer is used. It has been stated in previous arti-

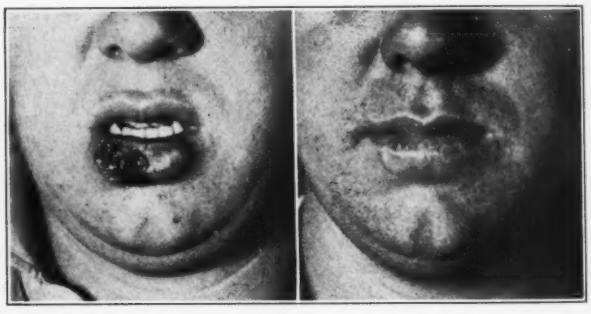

Fig. 1

Squamous cell carcinoma of the lower lip treated with x-rays only. The total dose was 4,380 r divided into five exposures. The second picture was made thirteen months after treatment. The cosmetic results are ideal.

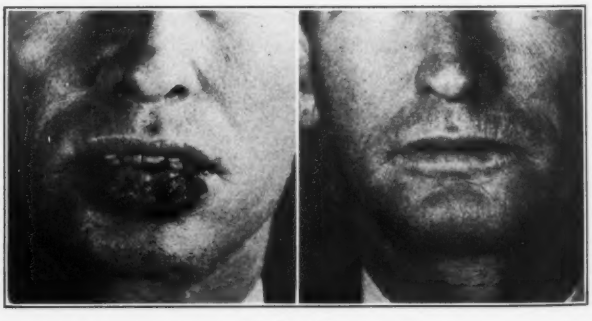

Fig. 2

Squamous cell carcinoma of the lower lip treated with x-rays only. The total dose was 4,456 r divided into six exposures. The clinical and cosmetic results are satisfactory.

cles[10] that metastases seldom develop as a result of carcinoma of the lower lip. Enlarged lymph nodes are frequently inflammatory processes that promptly disappear with the improvement of the lip lesion. When operable secondary lesions are evident and a competent surgeon is available, a block dissection is advisable. The indications for operation will be discussed at the close of this paper.

INTRA-ORAL CANCER

Our success in the treatment of carcinoma of the face and lower lip with radiation induced us to seek a method that would produce similar results in the mouth. The early x-ray technic in this region was not very helpful. The use of interstitial steel radium needles promised something, but the needles were too large, contained too much radium, and the filtration was inadequate. The use of weak platinum radium needles, as advocated by Regaud and others in the treatment of tumors involving the cheek, alveolar margins, anterior pillars, tongue and floor of the mouth, has greatly improved our radiation technic in these areas. Radon seeds are efficient in the treatment of these regions, but since we are unable to obtain them promptly, the platinum filtered radium needles are regularly used. The needles[11] are placed around and beneath the growing edges of the tumor, spacing them about 1 cm. apart. Each needle is sutured in place and the attached thread is brought outside of the mouth. When all needles are in place the threads are twisted together and tied to a linen label on which is printed in red ink, *"Radium; Don't Throw Away."* As a

Fig. 3

Extensive squamous cell carcinoma of the lower lip without evidence of metastases. Tumor mass removed with the endotherm knife. Treated with implanted platinum needles. The scarring is due to the large amount of tissue removed. He is clinically well.

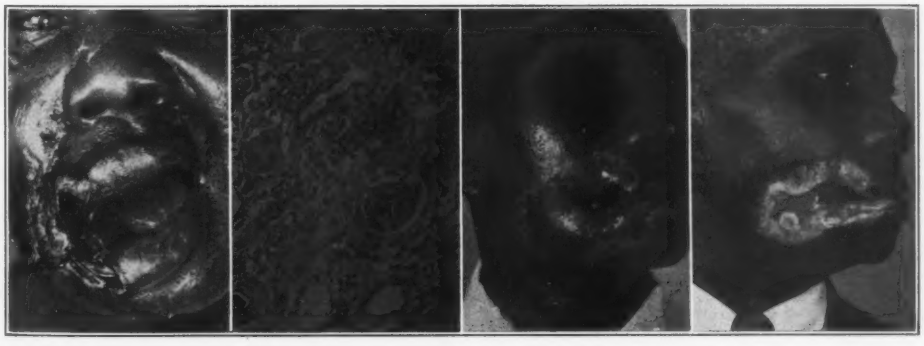

Fig. 4

Extensive epidermoid carcinoma on the inside of the cheek and extending into the corner of the mouth, involving the skin. Treatment was by implanted platinum radium needles and a modified Coutard technic. The tumor melted away promptly. The rather extensive x-ray dermatitis in the skin is healing nicely.

rule the implantations are done under local anesthesia. After all of the needles have been inserted, a radiograph is made for the purpose of studying the needle patterns. If the distribution of the needles is not correct, one or more may be changed. In most cases the needles are left in place for seven days, during which time it is necessary to pay particular attention to oral hygiene and diet. Pain is usually not a troublesome symptom after the first few hours. After the needles are removed, the tumor usually regresses rapidly, leaving a white membranous reaction which is superficial and clears away after a few weeks. A clean granulating surface remains and healing occurs in two or three months. A soft, pliable scar results and interferes little or not at all with the functions of the mouth. In tongue lesions, the taste is not disturbed and mobility is not impaired. Bony structures lying near the radium needles show little or no damage, although occasionally flakes of bone may separate. Large tumors involving the hard palate, such as the one shown in *Fig. 6*, have disappeared promptly without any bone damage. For a more complete discussion of the subject of intra-oral carcinoma, reference is made to previous articles.[12] Our experience is now nearing the five-year period and we hope soon to have something to say about five-year cures.

CANCER OF THE PHARYNX AND LARYNX

Carcinoma in the pharynx and larynx is a condition in which surgery has been relatively unsuccessful. This subject has been discussed in some detail by me[16] and will not be considered further here. With the advent of interstitial radium therapy, various plans were worked out for implanting the relatively inaccessible tumors of the pharynx and larynx, and radon seeds were obviously better than needles for this type of work. Although some good results were obtained, much difficulty was experienced in evenly irradiating the large tumors. It was found that distressing reactions in the cartilage of the larynx limited the dose of radiation in this region. The internal irradiation was augmented by radium packs and a massive dose x-ray technic, but the external irradiation did not assume a role of major importance until Coutard[15] elaborated his method, whereby large, efficient doses could be delivered to the mid-line of the throat without the production of serious injuries to the normal tissues. This made it possible to rely on deep x-rays alone, and the present tendency is to eliminate implanted radium in the treatment of the deeply seated tumors. Fortunately, the carcinomas of the pharynx and larynx are much more radiosensitive than their histology would indicate, and they do not require doses as large as those needed for the epithelial neoplasms of the mouth. Though efficient, Coutard's technic was not practical in private practice because of the length of time required to give a treatment (one to two hours). After reviewing the technic used by Lenz, Coakley and Stout, and Martin and McNattin, we have adopted a modified Coutard technic similar to that used by Merritt in Washington, District of Columbia, which utilizes 220 kv. peak, a filter of 2.25 mm. copper and 1 mm. aluminum, 20 milliamperes, and a target skin distance of 50 cm. Of the many modifications of the original Coutard plan, this technic promises to be the most efficient at the present time. The areas exposed measure from 7 to 15 cm. on a side, and the dose ranges from 200 to 300 r measured in air. The total dosage over each skin area ranges from 2,000 r to 3,500 r. The dermatitis occasioned by this treatment on the outside and the epithelitis on the mucous membrane on the inside are considerable. Usually the epithelitis appears first and likewise disappears before the superficial dermatitis begins to clear up. Patients begin to complain of soreness in the throat from nine to twelve days from the time treatment begins. Examination of the throat will reveal spots of superficial ulceration and white membranous patches on the mucous membrane of the soft palate. As this condition spreads to the walls of the pharynx, swallowing becomes painful. During this stage the patient must have careful attention. The saliva becomes thick and it is often difficult to keep the air passages free. Nourishing liquid food in sufficient quantities is necessary. After ten to fourteen days the reaction in the throat improves and the patient becomes more comfortable. There will be itching and burning over the denuded skin which is usually combated with applications of boric ointment. Healing of the skin requires from three to six weeks. In favorable cases, regression of the tumor begins with the appearance of the epithelitis and should be complete in from three to four weeks. In the successful cases it is often difficult to find evidence of the original site of the lesion after the mucous membrane heals.

CERVICAL METASTASES

In the treatment of carcinoma in and about the mouth, prophylactic high voltage radiation is given over the areas where metastases are

most likely to appear. When operable secondary lesions are evident, and a competent surgeon is available, a block dissection is advisable. If, however, the case is not operable and the nodes are of moderate size, Quick inserts radon seeds into the individual nodes after exposing them at operation. The small platinum radium needles may be used in the same way. When the masses in the neck reach a considerable size, satisfactory reduction can frequently be obtained by inserting parallel rows of long platinum, radium needles in the base of each tumor at 1 cm. intervals for a period of seven or eight days. This procedure can be safely augmented by doses of deep x-rays totaling 1,800 to 2,000 r and given at the rate of 300 r per day. The more embryonic tumors of this type show an excellent response to this form of therapy, and even those containing more adult cells are reduced in size and may remain quiescent for many months. Malignant tumors of the pharynx metastasize to the cervical lymph nodes, and what has been said regarding the treatment applies to secondary lesions from the pharynx and larynx. It is worth while to mention the fact that in cancer of the pharynx the first evidence the patient has of the disease may be enlarged glands of the neck. In many instances these metastatic nodes are more resistant to radiation than the primary lesions, and doses which clear the throat of all pathologic tissue may cause only partial regression of the involved nodes. If they are still palpable after four weeks, Hayes Martin recommends that they be implanted with radon seeds. If seeds are not available, weak, platinum radium needles may be equally serviceable. When large masses are present in the neck, and the tumor is not extremely anaplastic, it is our custom to insert platinum needles measuring 5 cm. in length beneath the involved areas. These needles are placed parallel to one another at intervals of 1 to 1.5 cm. and left in place for seven to eight days. They have a wall thickness of 0.6 mm. and contain 0.6 mg. of radium element per centimeter of active length. Divided doses of deep x-rays, totaling about 2,000 r, are given over the same region, and this treatment is started while the needles are in place. This procedure produces a rather severe skin reaction, but the results seem to justify it.

CASE REPORTS

The following case reports, briefly outlining the conditions as they appeared and the technic used in their treatment, will, we believe, be of interest to those doing radiation therapy:

Case 1.—A young man 23 years old noticed a hard, tender area on the right side of the lower lip nine months before he presented himself for examination. The lesion grew slowly until about three months before his first visit, when it took on a rapid growth, became painful on pressure and ulcerated in the center. Examination revealed a distinctly indurated mass, twenty mm. in diameter, that was covered with a thick, dirty crust from beneath which a thick, creamy pus exuded. No evidence of glandular involvement could be found. He was an inveterate smoker.

The treatment consisted of five x-ray exposures with the following factors: 70 kv. peak, 5 ma., 10 minutes, 10-inch target skin distance with a filter of ½ mm. of aluminum and repeated every forty-eight hours. The area exposed was 25 mm. in diameter. The number of r units per treatment measured in air was 876. As a result of this treatment, there was an active destruction of the superficial tissue, causing an ulcerated area over the growth which lasted about three weeks. At the end of six weeks this area had healed completely without leaving any evidence of the carcinomatous growth. The second picture in *Fig. 1* shows the results of x-ray treatment in this case.

Case 2.—This patient was a small, well nourished man, 45 years of age at the time he consulted us about a growth on the lower lip. For twenty years his lip had never been free of a crust. About a year previously a small, hard lump appeared in the center of the lip. This growth slowly increased in size until more than two-thirds of the lip was involved. Because he had not experienced any pain he was not alarmed about his condition. His fellow workers began to object to his association. Fear of losing his job, more than anything else, induced him to apply for treatment.

Examination revealed an ulcerating mass covering the greater part of the lower lip. The growth was covered with many small crusts that gave it a cauliflower appearance. The induration extended down into the subcutaneous tissues. Bleeding was noticeable, due to breaking of the crusts when moving the lip. The lymph nodes were not involved. The discharges were mucopurulent and the odor was very offensive. He had been a heavy smoker for many years.

The treatment was the same as in *Case 1*, except that in this case there were six x-ray exposures and a larger area was covered. The tumor was completely destroyed. There is no scar, fibrosis or atrophy, and the tissues covering the lip are perfectly normal in appearance. The second picture in *Fig. 2* was made about a year after treatment. This patient was also cured of his tobacco habit, has gained twenty pounds in weight and still holds his job. Biopsies were not done in *Cases 1* and *2*, because the appearance of the lesions, together with their histories, was conclusive.

Case 3.—A farmer 72 years old and in fairly good general health first noticed a small, warty growth in the left corner of the mouth about twenty years before he came to me. The changes in the growth were scarcely noticeable until about eight months before, when it began rapidly to increase in size. Examination revealed a cauliflower tumor that covered the entire lower lip. The ulcer was raw, repulsive, and the edges were indurated with a tendency to roll inward. The pathological report was epidermoid carcinoma, Grade 1. The treatment in this case was begun by removing the greater part of the cancerous mass with the endotherm knife. This was followed by the implantation of nine 1.33

mg. and one 2.4 mg. platinum needles. The needles were inserted under the edges of the tumor about 1 cm. apart and firmly sewed in position, where they were allowed to remain for seven days. No evidence of enlarged lymph nodes could be made out. Contrary to our usual methods, no x-rays were used in this case. There is considerable deformity on the left side of the lip, occasioned by the removal of the tumor mass with the endotherm knife. While he was clinically well at the last observation, the time is too short for final judgment in this case.

Case 4.—The subject of this report is a negro man 56 years of age, well developed, and in good general health. About a year before coming to me he noticed a small blister on the inside of the right cheek. At the site of the blister a tumor slowly developed which covered the inside of the cheek and extended into the corner of the mouth. Examination showed a large carcinomatous mass involving the upper and lower lip at the corner of the mouth, and extending well back on the inside of the cheek. The cheek was distinctly indurated. The laboratory report was epidermoid carcinoma, Grade 3. The skin was only slightly involved at the corner of the mouth, which was partially destroyed. The negro's skin is, to a remarkable degree, immune to carcinoma. During a residence in the South of forty-three years the author has never seen a case of primary carcinoma of the skin in a full-blooded negro.

The treatment consisted of the implantation of ten 1.33 mg. and eleven 2.4 mg. platinum radium needles under and around the tumor for seven days. To the effect of the radium needles was added 2,100 r units of high voltage x-radiation over the side of the face during a period of seven days. The x-ray treatment was given while the needles were in the tissues. A marked dermatitis developed on the outside of the cheek and to a lesser degree on the side of the neck. This reaction healed rapidly, and the side of the face was practically well at the end of six weeks. The tumor on the inside of the cheek completely disintegrated, leaving the mucous membrane smooth and with very little evidence of the cancerous growth.

Case 5.—The subject of this report was a poorly nourished man, 82 years old, who had used tobacco for sixty years. He complained of a non-painful tumor on the side of the tongue that interfered with talking and eating. On examination, we found a round, firm, elevated carcinomatous mass near the middle of the left side of the tongue and about 25 mm. in diameter. A similar tumor measuring 7 by 25 mm. was found beneath the right side of the tongue near the floor of the mouth. No enlarged glands could be felt in the mouth or in the neck. The report from the laboratory was epidermoid carcinoma, Grade 2.

The treatment was begun by implanting eight 0.6 mg. platinum radium needles around the tumor on the left side of the tongue. Three 1.33 mg. and two 0.6 mg. needles were inserted under the lesion on the floor of the mouth on the right side, and three 1.33 mg. and four 2.4 mg. needles were placed in the submental areas. All of the needles were firmly sewed in place and allowed to remain for seven days. The effect of the radium needles was supplemented by 900 r units of high voltage radiation to each side of the neck over a period of seven days. The final results of this treatment were satisfactory. He has been well for more than a year, has gained weight, and is much improved in a general way.

Case 6.—The subject of this history is a man 62 years old, in good general health, and a watchmaker by trade. For twenty-five years he has noticed a round tumor in the roof of the mouth. Its growth was slow, but it finally occupied almost the entire palate on the

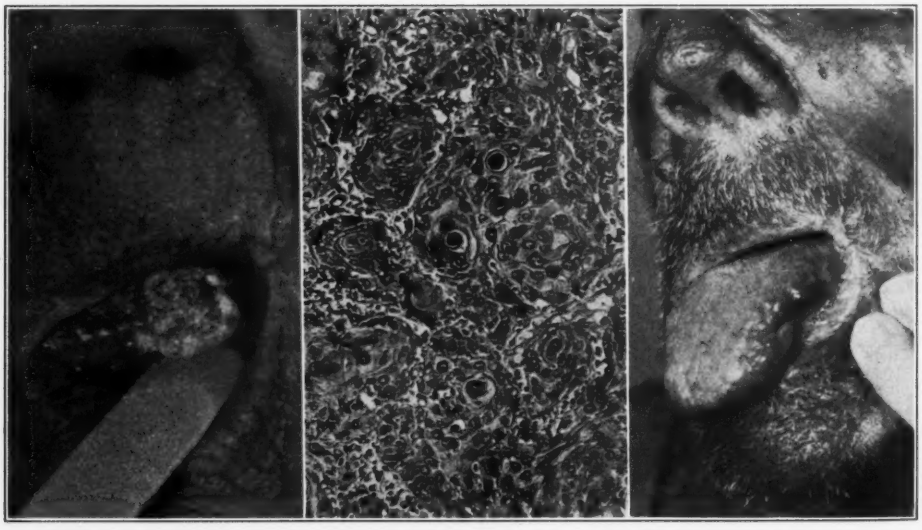

Fig. 5

Epidermoid carcinoma of the tongue without evidence of metastases. Treatment was by implanted platinum radium needles in the tongue and Coutard x-ray therapy to the sides of the face and neck. Results are satisfactory.

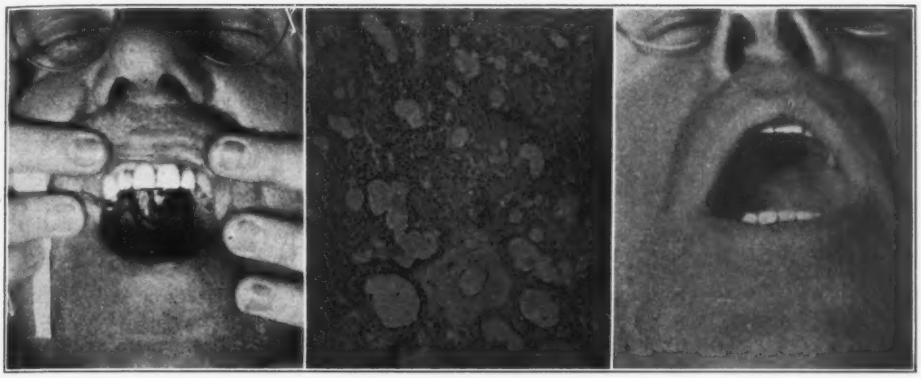

Fig. 6
Mixed tumor of the hard and soft palate treated with platinum radium needles. Regression was complete and there is practically no scar as evidence of the former lesion.

right side. There was never any pain. On examination, the mass measured 44 mm. in length and 25.5 mm. in width. The growth arose from the right side of the hard palate and extended well back into the soft palate. The tumor was well beneath the mucous membrane except for an ulcerated area in its anterior portion. His mouth had an unusually high arch, into which the tumor was snugly fitted. The laboratory diagnosis was: "mixed tumor."

The treatment of this case was by interstitial radiation. Three 2.4 mg., four 1.33 mg. and two 0.6 mg. platinum radium needles were inserted into the tumor for seven days. The tumor was completely destroyed. The surface of the palate is smooth and the result of the treatment is entirely satisfactory. Although the neoplasm was benign, its large endothelial lined spaces apparently responded well to radiation.

Case 7.—A man 60 years of age came to Baylor Hospital complaining of increasing hoarseness and some discomfort in the throat. A laryngoscopic examination done by Dr. Abell Hardin revealed a tumor involving the left vocal cord. A piece of the tumor was removed and diagnosed as squamous cell carcinoma. During a period of two weeks 3,900 r was administered to the sides of the neck through portals measuring 10 cm. by 8 cm. Although this dosage was low, the patient who had a short thick neck, developed much difficulty with swallowing and the treatment was stopped. An examination done three months after the cessation of treatment showed no evidence of the tumor, but the left vocal cord was partially destroyed. He felt quite well and his hoarseness had disappeared. At the end of one year and four months the patient remains symptom-free and Dr. Hardin states that no evidence of a recurrence can be made out.

RESULTS

Radiation, in the treatment of the lower lip, has passed the experimental stage. During an experience of thirty years we have treated several hundred cases with results similar to those shown in *Figs. 1* and *2*. Figures covering the percentage of actual cures have been published in previous articles.[10]

Now that we have better radium facilities and an improved x-ray technic, we are more hopeful of improved statistics for cancer on the inside of the mouth. Malignancy of the tongue has always been a difficult disease to handle. If perchance removal of the tongue cured the cancer, the patient was inconvenienced from the mutilation for the rest of his life. The excellent cosmetic and functional results obtained with radiation are illustrated in *Fig. 5* and furnish ample proof of the superiority of the method. Coutard reported 20 per cent of five-year cures resulting from the use of his x-ray technic in the treatment of 212 cases of cancer of the pharynx and larynx. Radiation has become the method of choice for this region. Although our experience covers a period of only a little over two years, we are impressed with the wonderful possibilities of this method.

SUMMARY

Actual results indicate that irradiation, when the newer technics are used, constitutes the method of choice in the treatment of cancer of the lip, mouth and throat.

BIBLIOGRAPHY

1. Pusey, William Allen: Roentgen Rays in the Treatment of Skin Diseases. J.A.M.A., **37**:820, Sept. 28, 1901.
2. Pusey, William Allen: Case of Sarcoma and Hodgkin's Disease Treated by Exposures to X-Rays: A Preliminary Report. J.A.M.A., **38**:166, Jan. 18, 1902.
3. Pusey, William Allen: Report of Cases Treated with Roentgen Rays. J.A.M.A., **38**:909, April 12, 1902.
4. Pusey, William Allen: A Subsequent Report on a Case of Carcinoma Discharged as Hopeless and Reported as a Failure. J.A.M.A., **39**:487, Aug. 30, 1902.
5. Pusey, William Allen: The Rationale and the Indications for the Therapeutic Use of Roentgen Rays. Jour. Cut. Dis., N. Y., Aug., 1903.

6. Pusey, William Allen: Radium and Its Therapeutic Possibilities. J.A.M.A., **43**:173, July 16, 1934.
7. Pusey, William Allen: Therapeutic Use of X-Rays Three Years After. J.A.M.A., **44**:1496, May 13, 1905.
8. Martin, James M.; and Martin, Chas. L.: Fractional Dose Method in X-Ray Treatment of Skin Malignancies. Sou. Med. Jour., **17**:391-7, June, 1924.
9. Martin, James M.: X-Ray Therapy in Skin Malignancies. Radiology, **8**:204-14, March, 1927.
10. Martin, James M.: Rational Therapy in the Treatment of Cancer of the Mouth and Lips. Radiology, **16**:881, June, 1931.
11. Martin, James M.: Conservative Treatment of Cancer of the Mouth and Lip. Southwestern Med., Oct., 1931.
12. Martin, Chas. L.; and Martin, James M.: Cancer in and About the Mouth Treated with Irradiation by the European Method. Texas State Jour. Med., **104**:286-290, Aug., 1931.
13. Martin, Chas. L.: Treatment of Malignant Tumors. J.A.M.A., **99**:1587-91, Nov. 5, 1932.
14. Martin, Chas. L.: Carcinoma of the Lip and Mouth. Radiology, **22**:136-46, Feb., 1934.
15. Martin, James M.; and Martin, Chas. L.: Modified Coutard Roentgen Therapy. J.A.M.A., **104**:605-608, Feb. 23, 1935.
16. Martin, Chas. L.: Irradiation Therapy of Malignant Tumors of the Oral Cavity, Eye, Ear, Nose and Throat. Ann. Otol., Rhinol. & Laryngol., **44**:426, June, 1935.
17. Martin, Chas. L.: Carcinoma in the Upper Pharynx. Amer. Jour. Surg., **30**:36-45, Oct., 1935.

DISCUSSION (*Abstract*)

Dr. Fred M. Hodges, Richmond, Va.—Dr. Martin has given us a very thorough and complete demonstration of just what can be accomplished in cancer of the lip, oral cavity, larynx, and so on. Those of us who have been in this work a long time recognize Dr. Martin not only as a pioneer in this work, but as one of the very first in America to recognize the fact that enormous doses of irradiation were necessary if these cases were to be cured. I personally use a different technic in cancer of the lip, in that I employ one enormous dose instead of the fractional method used by Dr. Martin, but certainly none of us can show any better results than he has obtained. In intra-oral and laryngeal carcinoma we follow just about the technic which was outlined by Dr. Martin.

I wish very strongly to emphasize the point that regardless of the size or grade of a tumor enough irradiation should be employed to be certain that radio-resistant malignant cells will be destroyed. A maximum dose, that is, all that the surrounding normal tissues can stand, should be used in every instance, since not infrequently a lesion is of the mixed type where sections from different portions of the tumor may show different histological gradings.

Dr. Martin's statement that the majority of radiologists and dermatologists are still giving insufficient dosage is certainly borne out in my experience. His many papers and excellent exhibits on the treatment of cancer have not only saved many lives, but have caused many radiologists and dermatologists largely to lose the great fear of over treating and burning these patients. The large majority of the mistakes made by all of us in the past have been due to under treatment, not over treatment.

Dr. Martin (closing).—While Dr. Hodges' technic differs somewhat from mine, he recognizes the important factors necessary in the successful conduct of radiation therapy in the treatment of cancer.

Fortunately, radiation therapy is somewhat elastic and may be varied to suit individual conditions, remembering always that the total amount of radiation delivered to the tissues must be sufficient to destroy all cancer cells without doing irreparable damage to the surrounding normal tissues.

I am pleased to have Dr. Hodges endorse my statement that "the majority of radiologists and dermatologists are still not giving their advanced cancer cases a sufficient amount of radiation to produce successful cures." In order not to be misunderstood, I want to sound a note of warning to all inexperienced men using radiation methods not to go to the other extreme with an undetermined technic and do irreparable damage to the tissues and the cause of radiation much harm.

THE ROLE OF RADIATION THERAPY IN THE TREATMENT OF INOPERABLE DEEP-SEATED ABDOMINAL MALIGNANCIES*

WITH REPORT OF A CASE OF ADENOCARCINOMA OF THE STOMACH

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All physicians and even many of the laity are superficially acquainted with the fact that the x-rays and radium are successfully employed in the treatment of cancer, but this broad knowledge must be supplemented from time to time by ever-changing methods, improvements in technic of application and new and increasing uses. It is not our desire to recapitulate here the role radiotherapy has played during the past twenty-five years, but we do wish to bring to your attention a phase which we believe has been overlooked, namely: the treatment of inoperable deep-seated abdominal malignancies or those of doubtful operability or etiology.

In this group the term inoperability applies both to tumors which were obviously inoperable and in which no operation was performed, and to those discovered to be inoperable on exploration. All non-resectable tumors are considered inoperable here, even though palliative operations, such as gastro-enterostomies, were possible. The term, operative mortality, applies to that group which became much worse immediately following operation and died in the hospital a short time thereafter. This postoperative period has been limited to three weeks in this series.

Recently, more and more importance has been attached to the preoperative irradiation of many tumors, chiefly those of the breast, kidney and some bone tumors, and the results, broadly

*Read in General Clinical Session, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

Chart 1

GASTRO-INTESTINAL CARCINOMAS
1934

	Union Memorial Hospital				Johns Hopkins Hospital			
	No. of Cases	Operable No. and Per Ct.	Inoperable No. and Per Ct.	Operative Mortality No. and Per Ct.	No. of Cases	Operable No. and Per Ct.	Inoperable No. and Per Ct.	Operative Mortality No. and Per Ct.
Stomach	12	6—50	6—50	2—33	29	7—24	22—76	0
Colon	14	10—70	4—30	4—36	18	11—61	7—39	3—25
Rectum	10	4—40	6—60	1—17	24	8—34	16—66	1— 7

speaking, would seem to justify this procedure. Irradiation of abdominal tumors has heretofore never aroused any particular degree of enthusiasm, but the improvements in technic, higher voltages, increasing knowledge of filtration, the more accurate methods of measuring surface and depth dosages, and especially newer knowledge concerning the radiosensitivity and classification of tumors, would lead one to believe that radiotherapy will assume a position in this field similar to that which it occupies in various others.

Why have our results in the treatment of abdominal cancer by irradiation been unsatisfactory? Probably for two reasons: first, the lack of knowledge concerning radiosensitivity of tumors; and second, the difficulty of applying radiation to abdominal tumors without too great shock to the patient. This has very largely been overcome by small protracted daily doses over long periods of time.

I am sure we are all still of the opinion that radical resection in cancer is the method of choice, but there are many cases in which nothing is ever done and the patient is sent home without any palliative treatment. Merritt,[1] ourselves, and others, have already found and reported instances where inoperable abdominal tumors have been rendered operable. A careful perusal of statistics on gastro-intestinal cancers from the Union Memorial Hospital, Baltimore, the Johns Hopkins Hospital, and the Mayo Clinic reveal some interesting though discouraging results.

Chart 2

UNION MEMORIAL HOSPITAL*
1922-1934

Carcinoma of the Colon and Rectum

Number of cases	204
Operable	54 %
Operative mortality	22.5%

*Dr. S. McLanahan, Jr. (personal communication).

The analyses of the statistics of the Johns Hopkins Hospital, the Mayo Clinic and elsewhere indicate that approximately 50 per cent of all carcinomas of the gastro-intestinal tract are inoperable with an operative mortality of 21

Chart 3

JOHNS HOPKINS HOSPITAL*
1889-1935

Carcinoma of the Colon	
Number of cases	192
Operable	53.6%
Operative mortality	26.8%
Carcinoma of the Rectum	
Number of cases	319
Operable	36.7%
Operative Mortality	22.2%

*Raiford, T. S.: Ann. Surg., **101**:863-885, 1042-1050, March and April, 1935.

Chart 4

MAYO CLINIC
Gastro-Intestinal Carcinoma

	Operable Per Ct.	Inoperable Per Cent	Operative Mortality Per Ct.
Stomach: Balfour, 1934	45	55	*10
Colon: Rankin, 1931	56	44	9.1
Rectum: Rankin, 1927	40	60	5-15

*In a recent series of 200, 5 per cent.

Chart 5

RATE OF RESECTABILITY OF CARCINOMA OF THE ALIMENTARY TRACT*

Situation of Carcinoma	Patients Operated Upon	Subjected to Resection	Per Cent
Esophagus	0	0	0
Stomach	271	125	46
Small intestine	8	6	75
Large intestine	168	84	50
Rectum	* 152	89	58
Total	599	304	50

*Balfour, D. C.: Collected papers of the Mayo Clinic, 1934.

Chart 6

CARCINOMA OF STOMACH

Distribution of Gross Types According to Broders' Index*

Grades	Fungating Carcinoma	Ulcerating Carcinoma	Infiltrating Carcinoma	Total
I	2— 9 per cent	1—3.5 per cent	0	3—3.1 per cent
II	7—31.8 per cent	7—25 per cent	0	14—14.7 per cent
III	10—45.4 per cent	11—40 per cent	15—33.3 per cent	36—38 per cent
IV	3—13.8 per cent	9—32.5 per cent	30—66.6 per cent	42—44.2 per cent

*Whipple and Raiford: Surg., Gyn. & Obst., **59**:397-409, 1934.

per cent. The resectable cases without distant involvement yielded 23 per cent of five-year cures. A summary of the above statistics shows that only about 9 per cent of the patients suffering from gastric cancer live five years.

The surgeon is placed in the unfortunate position of seeing most of his patients in an advanced stage of malignancy upon their first visit, and until public education results in earlier and periodic visits to the physician, his success will be no greater.

In Whipple and Raiford's[2] series it was found that approximately 38 per cent of gastric cancers fell into Grade III and 44.2 per cent into Grade IV. Going still further it was found, from various statistics, that of all gastro-intestinal cancers about 31 per cent belong in Grade III and 22 per cent in Grade IV. Therefore, it is reasonable to suppose that many cancers of the stomach, colon and rectum are radiosensitive to a more or less degree than was generally supposed and, if this be true, one is forced to the conclusion that radiotherapy is destined to play an increasingly prominent role in this problem.

Pack's[3] statement that the majority of cancers of the stomach are radioresistant, only about 10 per cent showing clinical improvement after irradiation in his series, may be explained by the possibility that he refers only to the inoperable gastric tumors treated in his series by this means. If this is true it is possible that a large percentage of his gastric tumors may have been Grades I, II and low III.

Pack is, however, of the opinion that the ulcero-cancers, the diffuse superficial cancers, the papillary and polypoid types, and the bulky adenocarcinomas occurring especially in the fundus and cardia regress after careful irradiation.

Chart 7

CARCINOMA OF COLON, RECTOSIGMOID AND RECTUM*

With Regional Node Involvement	Grade I Per Ct.	Grade II Per Ct.	Grade III Per Ct.	Grade IV Per Ct.
Broders' classification	9	51	28	12
Five-year cures	44	34	13	15
Without Regional Node Involvement				
Broders' classification	16	62	16	6
Five-year cures	69	56	49	37

*Rankin: J.A.M.A., **101**:491-495, 1933.

Chart 8

CARCINOMA OF THE CERVIX

WERTHEIM OPERATION

Living Five Years or More*

		Healy, 1925-1926 Memorial Hospital, New York Per Cent	Martzloff Johns Hopkins Hospital Per Cent	Broders Mayo Clinic Per Cent
Grade I	Early and borderline	50 Radiation	47+ Surgery	53.33 Surgery
	Advanced	4 "	—	—
Grade II	Early and borderline	43 Radiation	24 Surgery	21.5 Surgery
	Advanced	14 "	—	—
Grade III	Early and borderline	66 Radiation	9.5 Surgery	9.5 Surgery
	Advanced	42 "	—	—

*Healy, W. P.: Radiology, **13**:323, 1929.
Martzloff, K. H.: Johns Hop. Hosp. Bull., **40**:160, 1927.
Broder: personal communication quoted by Martzloff.

Therefore, it seems logical, all things being considered, that cancers in the upper portion of the stomach should be submitted to irradiation, not only because of their comparative radiosensitivity, but also because of the fact that total or radical subtotal gastrectomies, which are necessary, are associated with an exceedingly high operative mortality.

Ewing[4] has recorded a small cell type of cancer originating in the base of the gastric glands, some of which are anaplastic, resembling lymphosarcoma in their structure, and which are radiosensitive. All of which definitely indicates that many gastric cancers are influenced to varying degrees by irradiation.

Whipple and Raiford have gone a step further in trying to determine and group the possible degree of malignancy from the duration of the symptoms which first bring the patient to the physician. Using Broders' classification as a basis, they found that in Grades I and II symptoms began seven to eight months before the patient sought advice from a physician. Grades III and IV, in general, gave symptoms for eight or nine months, but in these two groups, if those giving typical ulcer histories were segregated, it was found that the average duration of symptoms of all cases was over twenty months, but that the duration of symptoms after segregating the typical ulcer cases averaged about six months for Grade III and four months for Grade IV. In other words, patients who give a history of rapid fulminating carcinoma are most apt to harbor a growth of relatively greater malignancy, while those who give a history of gastric ulcer with slow progress, which does not respond to conservative treatment, likewise are apt to fall into Grades I and II. Therefore, one is led to the opinion that those falling into Grades III and IV should be subjected to irradiation whenever serious doubt as to operability exists.

The character of deeply seated abdominal malignant disease is often such as to defy every known method of scientific investigation. The time-honored surgical exploration of the abdomen as the primary step in the treatment of abdominal masses of uncertain etiology or operability may, we believe, be obviated in some cases by preoperative irradiation.

Roentgen irradiation of inoperable abdominal tumors or masses of uncertain origin has not yet reached the stage which provides for positive evaluation, but rapidly accumulating evidence would seem to indicate that it is to play an important role in the preoperative, postoperative and palliative treatment of inoperable abdominal malignancies.

At one time there was relatively little hope for success in the treatment of carcinoma of the cervix of the uterus (*Chart 8*). It is quite evident from the above statistics that surgery in this form of cancer is only comparable in effectiveness to irradiation in the very early and low degree of malignant types. It can in no way compare with the results with irradiation in the other groups. Radiation today has gone a very long way in dispelling this hopelessness. Probably there would be no basis for the hope of similarly brilliant results in the domain of gastro-intestinal irradiation, but certainly here is a fertile field which may yield the unexpected.

The tendency to radiation sickness during the treatment of these cases can now be largely overcome with the employment of higher filtrations and voltages and lower daily r input over a long period of time.

CONCLUSIONS

(1) Earlier diagnosis of carcinoma through continued education of the public and periodic examinations must be vigorously pushed. In the present state of our knowledge careful roentgenological studies using modern refinements of technic and clearer interpretation of early mucosal changes is the best available diagnostic method.

(2) Whenever clinical and/or roentgenologic findings indicate an early tumor, earliest possible operation is indicated.

(3) Whenever clinical and/or roentgenologic findings indicate definite inoperability or leave grave doubts as to operability, the lesion should be subjected to irradiation and subsequent x-ray examination may reveal that the tumor has become operable.

CASE REPORT

O. W. K., a white man, aged 43 (private patient of Dr. J. M. T. Finney, Jr.) was admitted to the Union Memorial Hospital August 23, 1934. He complained of pain in the epigastrium.

One year before admission he had had pain in the epigastrium, which was relieved by soda and food until February, 1934, when symptoms returned.

Gastric analysis showed free acidity 20, combined 10, and total 30.

The Wassermann reaction was negative.

Roentgen examination showed a filling defect at the

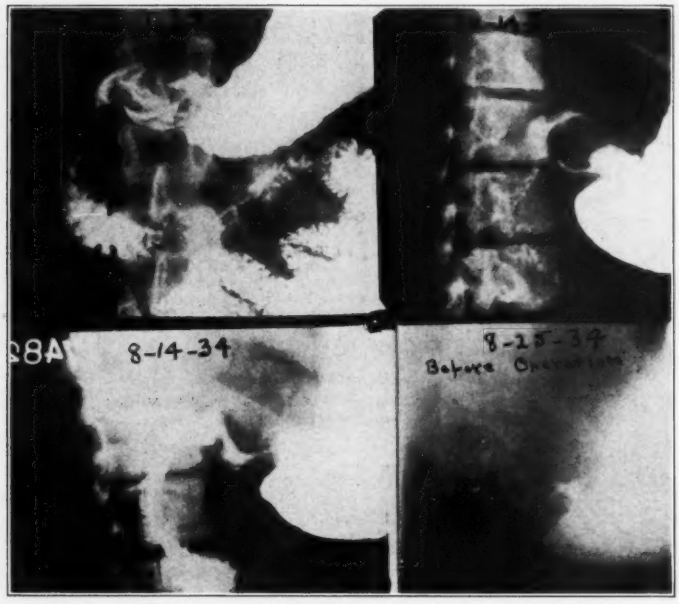

Fig. 1
Note the comparatively slow growth of the filling defect, yet it was a highly radiosensitive Grade III tumor.

pylorus extending well up along the lesser curvature (*Figs. 1, 2, 3 and 4*).

The first operation was done August 31, 1934. The omentum was thick, fatty and granular. The liver had a somewhat mottled granular appearance. There were no masses or nodules. The gallbladder was a little enlarged, but otherwise normal. There was a hard, rubbery mass involving the stomach in its entire circumference for about two inches at its pyloric end, which extended along the lesser curvature of the stomach to within two inches of the cardiac end of the stomach. Just above the upper limit of this mass and apparently not connected to it was a nodule in the stomach wall of the lesser curvature about the size of a hazel nut. The surface of this mass at the pyloric end on the anterior wall was white and smooth, and did not have the consistency of a carcinoma. On the stomach side the mass felt like a saddle-tree, but was also smooth. The gastrohepatic omentum was fastened down on the anterior superior surface

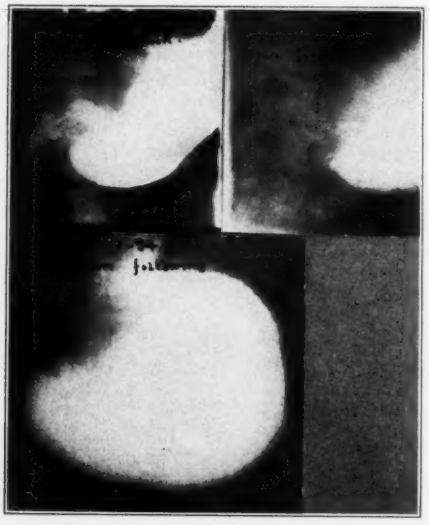

Fig. 2
Note the complete disappearance of the filling defect after irradiation.

Fig. 3
Normal functioning stomach after resection.

of the mass as if it had been blocking a perforated ulcer. No glands were felt anywhere in the abdomen.

The first course of irradiation was given September 17, 1934, to October 13, 1934. Two portals (10 x 10 cms.) over the anterior surface of the stomach were used, 200 k. v., 25 ma., 2 mm. copper and 1 mm. aluminum filtration. The focal skin distance was 50 cm., with daily doses of 200 r; 1,600 r were given through each portal.

He lost 8 pounds during the course of treatment. There was no anemia. He developed pyloric obstruction following irradiation, but without roentgenological evidence of a tumor. It was probably due to fibrosis.

The second operation was done January 19, 1935. The stomach presented quite a different appearance from that seen at the previous operation. Resection

Fig. 4

Drawing of the resected pyloric end of the stomach showing the carcinomatous infiltration along the superior border of the pyloric sphincter.

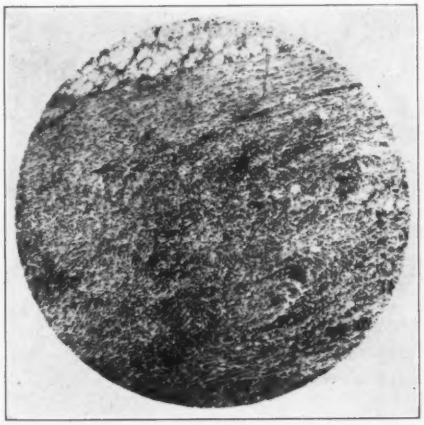

Fig. 5

Section from pyloric end of stomach. Note the distribution of carcinoma cells, marked diffuse fibrosis and mononuclear cell infiltration. The acinar arrangement of cells is absent. There is coagulation of both tumor and fibroblastic tissue; muscle cells show degeneration and distortion by fibrosis. The reaction is typical of changes seen after x-ray irradiation. Nuclei of tumor cell contracted into irregular deep-staining structures.

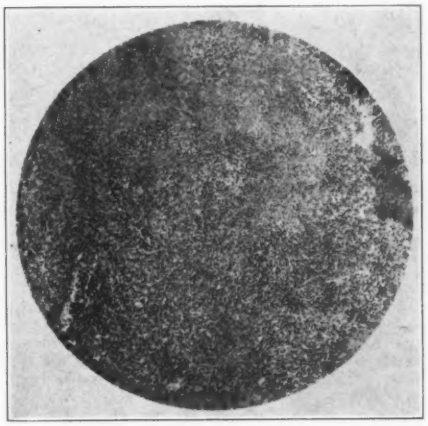

Fig. 6

Section from lymph node removed at operation. Note the extensive metastatic tissue and marked coagulation necrosis. Result of irradiation. There is also rather marked diffuse fibrosis.

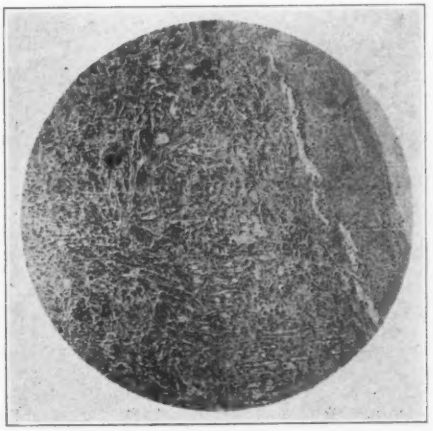

Fig. 7

Section obtained from implantation mass on wall of ileum (recurrence or metastasis after irradiation). Autopsy material. Note the acinar arrangement of cells, absence of fibrosis and necrosis. Cells are hyperchromatic and many contain colloid vacuoles in the cytoplasm. Typical adenocarcinoma with colloid changes.

of the pyloric end was decided upon with Polya closure. The stomach was thick walled, particularly at the pyloric end. The pyloric sphincter was partially occluded. There were several enlarged mesenteric lymph nodes close to the greater curvature of the stomach and many adhesions around the stomach. Recovery was uneventful.

Microscopic diagnosis was adenocarcinoma with colloid degeneration Grade III. Section from the pyloric end of the stomach and a lymph node showed a diffuse fibrosis and mononuclear infiltration. The acinar arrangement was absent. There was coagulation of the tumor and fibroblastic tissue. The reaction was typical of the changes seen after irradiation.

The second course of irradiation was given between December 4, 1934, and December 19, 1934. Two anterior portals were used as in the first series. Each was given 1,000 r, and 1 portal through the posterior aspect was given 600 r. The same factors were employed.

The third course of irradiation was given between February 11 and February 20, 1935. Through one anterior portal, 20 x 20 cm., 1,200 r were given. Through one posterior portal, 20 x 20 cm., 1,000 r were given. The same factors were employed.

Blood count February 19, 1935, showed 4,750,000 red cells, 4,200 white cells, and 90 per cent hemoglobin.

Death occurred on April 24, 1935.

Autopsy was done by Dr. Samuel Goodman with Dr. I. A. Nelson, pathologist, at St. John's Hospital, Tulsa, Oklahoma. The peritoneum was completely studded with small grayish miliary, discrete and coalescing flattened lesions, except where it was adherent to loops of intestines and omentum. All the loops of intestines were covered with the same lesions except where they were adherent. In some instances small locular collections of straw-colored fluid separated folds of intestines. Coalescence and induration were so marked in some areas that separation of intestinal loops was difficult. The omentum extended diagonally from over the spleen to the cecum which was lying about the level of the right superior iliac crest. The omentum was so indurated that it was difficult to pinch the thumb through it. The thickening was fairly uniform, varying from 2 to 4 cm. from edge to central portions. The omentum was particularly adherent about the region of a gastro-enterostomy which could be approached only from the mucosal surface of the stomach. There were some black silk thread sutures at the site of anastomosis. The infiltrating or indurating process did not seem to involve any structures except the omentum, peritoneum and mesentery of the small intestines. All other structures were free, even the wall of the stomach, duodenum, gallbladder and pancreas, which seemed to be involved at first, but which separated completely on careful dissection. On cutting through the indurated omentum, necrotic and caseous areas could be found measuring up to 4 or 5 mm. in their greatest dimension.

The lungs on both sides showed old, firm adhesions to the parietal pleura without thickening. There was no consolidation, congestion or other evidence of pulmonary disease. The heart and pericardium were normal. There were no mediastinal tumors, lymph nodes, induration or infiltrations. The pancreas weighed about 62 grams and showed no indurations, tumors or cysts. The adrenals were small, normally placed, nonhemorrhagic and of normal consistency. The liver weighed 1,600 grams with the capsule studded with the above described lesions, but the parenchyma appeared fairly normal on cut surface. The spleen weighed about 140 grams with capsule also studded, but the parenchyma showed no infarctions, indurations or other pathologic condition. The kidneys weighed about 120 grams each with capsules smooth and non-adherent, cortex and medulla sharply outlined. The ureters, bladder and prostate were normal.

Microscopic description by Dr. W. C. Merkel, pathologist, Union Memorial Hospital, Baltimore, follows: The section which was apparently obtained from the omentum shows a marked infiltration of adenocarcinomatous tissue. In the lesser scarred areas, the cells are arranged to form acini. The cells are hyperchromatic. Many of them show mitotic nuclei. Practically all of the lymphatics are plugged with neoplastic tissue. The paler stained cells show vacuoles which are translucent, displacing the nuclei to the periphery. The entire area shows a fibrous tissue stroma which is quite dense and undergoing hyaline degeneration.

The section of the liver appears practically normal. There is no evidence of fat, fibrosis or degeneration. No metastasis is encountered.

The section of the pancreas shows marked fibrosis, particularly in the central part of the lobules immediately surrounding the pancreatic ducts. The tissue is rather loose, indicative probably of a quite recent process. The peritoneal sheath of the pancreas is thick, scarred and infiltrated with tumor tissue, none of which is encountered throughout the pancreas.

The section of the intestine shows a mucosa and muscular wall. The peritoneal layer is thick and composed almost entirely of carcinomatous and scar tissue. The arrangement of the cells as well as the appearance of the cells plus the vacuoles are so typical of a gastro-intestinal carcinoma that the primary seat could readily be determined without any previous knowledge of its existence. One of the most interesting features is the marked dilatation of the lymphatics which are plugged with neoplastic tissue.

The section of the spleen shows hyperplasia, passive congestion and tumor tissue confined to the capsule. There is no evidence of invasion into the splenic pulp.

CONCLUSIONS

Inoperability was not determinable here until exploration. The fact that the tumor was rendered operable after the first course of irradiation indicates that preliminary irradiation might have obviated the first operation. The mechanical obstruction which followed this therapy was probably due to formation of fibrous tissue (in and around the pylorus). That we were treating a lymphoblastoma upon which a carcinoma became engrafted does not seem tenable in view of the microscopic and autopsy findings. Neither is there any basis for the belief that irradiation could have stimulated malignant epithelial cells. One is almost forced to conclude that the tumor was originally a slowly growing carcinoma.

REFERENCES

1. Merritt, E. A., Washington, D. C.; personal communication.
2. Whipple and Raiford: Surg., Gyn. & Obst., **59**:397-409, 1934.
3. Pack, G. T.: Sou. Med. Jour., **27**:747, 1934.
4. Ewing: Neoplastic Diseases. Philadelphia: W. B. Saunders & Co.

CARCINOMA OF THE SKIN IN ITS EARLY MANIFESTATIONS*

A CORRELATION OF CLINICAL AND MICROSCOPIC OBSERVATIONS WITH THE HYPOTHESIS OF ETIOLOGY IN SOMATIC MUTATION

By RICHARD L. SUTTON, JR., M.D.
Kansas City, Missouri

An epidermoid carcinoma of the skin begins as a very small anomaly. It enlarges by accumulation and accretion at the site of its commencement. As the quantity of abnormal cells increases, then, because of abnormal keratinization and desquamation, a scale is formed, which may drop off or be picked off and form again. The lesion may be imagined to have disappeared when a large accumulation of scale is at one time removed; but it grows back, because the living cells from which it was derived continue to reproduce. There is always inflammatory reaction in the corium underlying such an aggregate of abnormal epithelium, and into the round cell infiltrate the cancer cells erode and invade. In time, the total aggregate is gross in size, and palpable as a button-like, indurated disc. The scale becomes thicker in the center; soon it is increased by necrotic epithelial cells, leukocytes and exudate. The tiny lesion has become crateriform. It will bleed when the dry cap of detritus is torn off. Invasion progresses at the sides and underneath, so that an epithelioma is soon self-evidently manifest. Its deeper and wider extension, the continuation of destructive erosion, and metastasis are simply matters of time.

There are two ways of observing the process I have described. One is to follow a patient who comes for treatment of a cancer and has on his skin scaly patches and warty lesions. These may be watched as they evolve into gross cancers over a period of months or a few years. Every dermatologist in a favorable geographic location has done this, and will corroborate these facts. Another way is to excise from one or several patients lesions that seem to represent stages in this process of evolution, then study them microscopically. A complete bibliography of such observations is not necessary here. To this point in my argument, I believe substantiation by quoting others is superfluous. It has all been known for a generation or more. The interpretation of these phenomena is our chief interest.

I submit for your consideration the theory of mutation of somatic cells as originated by R. C. Whitman[1]. Hansemann[2] had presented a theory of "anaplasia" as the cause, which Whitman, with whom I agree, considers too vague a term. In view of the atypical mitoses, multipolar divisions, hyperchromatic and hypochromatic nuclei, asymmetric mitoses and changes in number of chromosomes, he[1] avers that the cancer cell is "a new kind of cell, strictly and literally a mutated cell." Actinic irritation, for example, notoriously a factor in the causation of skin cancer, does so by altering the process of cell division, so that true mutants arise, mutants which continue to reproduce, but are not responsive to whatever it is that keeps normal growth within normal bounds. If, in millions of epidermal mitoses, characteristics be so altered in only one instance as to produce a viable mutant cell unresponsive to normal restraints and capable of growing where normal cells do not grow, then a carcinoma might be started. The progeny of the one cancerous cell would constitute a colony growing parasitically, and with potentiality of ultimately resulting in death of the host.

Broders[3] states that "carcinoma, regardless of etiology, is a primary disease of the epithelial cells, and all other phases and sequelae, though of great importance, are in reality of secondary nature." In his careful study of small epidermal anomalies, he shows convincingly that cancer may be diagnosed while still of a thickness only little greater than that of normal epidermis. Small cancerous lesions began *de novo*, on previously unaltered skin, and the earliest visible manifestations are circumscribed dyskeratotic lesions which progress by continuous evolution into large and destructive tumors[4].

Molesworth[5], of Australia, has frequently pointed to the effect of sunlight upon the skin in the production of carcinoma. The lower lip is involved far more commonly than the upper because of its direction toward the sky. The dyskeratoses which become malignant occur most commonly on the exposed surfaces of sun-sensitive individuals.

The preponderance of skin cancer in poorly pigmented individuals is true of other animals than the human. Findlay[6] observed 190 cases in about one million cattle slaughtered in New South Wales. All but three of these were on partly or wholly white areas, and these three

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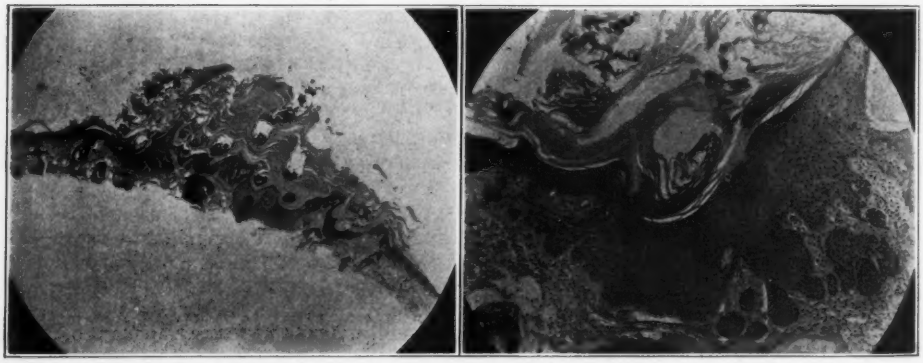
arose on the scars of brands. Roffo[7] successfully produced carcinomas in mice with ultraviolet irradiation.

Francis Carter Wood[8] points out that cancer grows best in healthiest tissue. This is what one would expect of tissue cells growing parasitically.

In Bowen's[9] disease, the lesions are typically circular or oval, beginning small and spreading centrifugally, then eventually crusting, burrowing, invading and becoming evidently malignant. Many senile keratoses have the structure of Bowen's disease, as Montgomery[10] states, a fact which my observations fully corroborate. Fraser[11] aptly remarks: "The cells in the Bowen lesion have already undergone the changes of malignant neoplasia." Intra-epithelial carcinoma, now a well recognized entity, possesses this same habit; cases have been described and discussed by J. R. Fraser, W. Freudenthal, J. Jadassohn, Borst[11] and many others. I shall present photomicrographs demonstrating the histologic evidences of intra-epidermal neoplasia. The early intradermal centrifugal spread of carcinoma is consistent with the hypothesis of a one-cell origin, the progeny of the one cell growing where they can grow, spreading within the epidermis, following the epithelium of the hair follicle, evoking a round-cell response in the dermis, then growing into this looser inflammatory tissue as into a culture medium. Ketron[12] described several curious examples of epithelioma forming annular lesions which had also begun in a small area, spread, then developed incrustations.

Malignancy in the cellular sense depends upon rate of growth, as J. C. Mottram[13] shows in his study of tar cancer. It is incorrect to allege that a lesion is simply benign or malignant in the strictest sense; it is either not neoplastic at all, or it is little, somewhat, quite, or very malignant, in accordance with its time rate of capacity for doing harm.

All arsenical keratoses, by some called "precanceroses," along with a host of other histologically independent lesions, possess a degree of malignancy in this rather mathematical sense. As Franseen and Taylor[14] show, about one-third of arsenical cancers are basal-celled, not being all squamous in character; but they all start as keratoses, though not all the keratoses possess enough *vis a tergo* to proliferate into ulcerative tumors. X-ray produces fairly comparable lesions. The scaly pigmented spots upon an irradiation atrophy are indistinguishable from senile keratoses. One notes, as Whitman[1] remarked, that all agents predisposing to cancer are those that are known to affect cells through their reproductive mechanism. I believe each keratosis represents a colony of progeny of an altered cell, a somatic mutant. The colony may be vigorous or weakly, malignant or abortive, hearty or asymptomatic. Perhaps a large proportion of mutated cells are non-viable and never



(A) (B)

Fig. 1

A keratosis from the helix of the ear of an elderly blond farmer.

(A) Topography of the lesion. The scale is produced by abnormal cornification of abnormal epithelial cells. Removal of such a scale removes a large proportion of the mass of the lesion, but does not alter the nature of the lesion.

(B) Higher magnification reveals retention of nuclei in the corneum; irregular thickening of the epidermis; alteration in epithelial cell type, the cells being large, irregular in size, variable in nuclear content, restless in appearance; budding outgrowths from the base and sides of the epithelial overgrowth; round cell infiltration of the dermis.

This lesion in time would undergo no fundamental change in pathology except progression and advancement. I believe it cancer as it stands, with present or future "malignancy" unaltered by mere increase in quantity.

give rise to naked eye lesions at all. Nevertheless, this theory is consonant with the facts, whatever belief it may be your pleasure to hold.

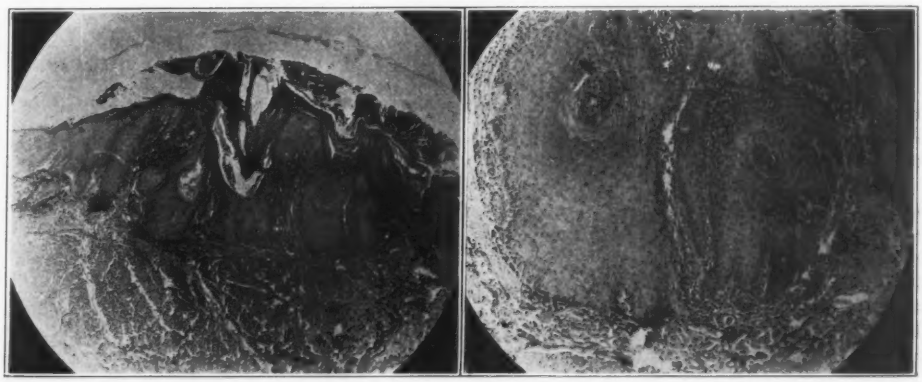
The blastomatoid changes that I stress as features of an early skin cancer have been observed and recorded in the epithelium of the uterine cervix, also squamous, by Schmitz and Benjamin[16], and by Schmitz, McJunkin and Macaluso[17]. The intra-epithelial spread of cancer of the cervix over the vaginal wall has been described by Eichenberg.[18]

I have elsewhere expressed my belief that the size of a lesion is not a criterion of whether it is cancer or not. Pennyweight or pound of tumor, the only difference is quantitative. The limit in smallness is plainly one cell; one solitary malignant cell which reaches the lung or liver, settles there and raises a family and so produces a nodule of cancer, possesses all the attributes of cancerousness within itself. As it floats in the blood, is filtered out by a narrow capillary, and digs in at that location, it may without apology be thought of as a cancer *per se*. M. B. Schmidt[19] in 1903 showed experimentally that only a few cancer cell emboli actually do take hold when an emulsion of them is injected intravenously, but each one that does is a satisfactory argument.

Rate of growth, as well as size, may vary a great deal, I believe, without affecting one's judgment of the basic nature of the pathologic process. We see one lesion which in six months attains the size that another reaches only after several years. The difference manifests itself histologically, so that differences stressed by Broders[20] in his grading of epidermoid carcinomas are generally valid in estimating malignancy, that is, capacity for harming the host, and likelihood of recurrence. However, Grade I or IV, the underlying nature of the process appears to be identical.

Rate of growth depends upon rate of cellular division. I would point out that the apparent rate of growth as observed clinically may be misleading. If a colony of cancer cells is growing at a constant rate so that the number doubles, let us say, in one month, then when the lesion is tiny its doubling in size is clinically not very apparent. In its early stages it is superficial, and relatively large proportions scale off and are lost. When, however, it attains the size of a cherry, and doubles that size in one month, the rate of growth would be said to be decidedly rapid. The aggregate would no longer lose a large proportion of itself each time it scaled off; its rate of growth might well be imagined clinically to have increased by leaps and bounds; and yet the rate in fact may not have changed at all.

It is seen clinically that, as soon as a scaly



(A) (B)

Fig. 2

A lesion of the lower lip that has required fifteen years to reach its present stage in development.

(A) Topography of the lesion. The epithelium is thick and irregular. On the lip, it normally possesses no downgrowths. The scale is abnormal corneum produced by abnormal epithelium.

(B) Higher magnification reveals "restless" outbudding from the epithelial masses; round cell infiltration of the corium; arrangement of epithelial cells in cornifying whorls; and irregular size of the epithelial cells, which are, most of them, much larger than is normal. The architecture is that of cancer.

The slow growth means low malignancy, but need not affect one's judgment of the basically blastomatous nature of the process. This is cancer of such slow rate of progression that it might never cause serious harm during the lifetime of the host.

so-called "precancerosis" becomes thick and invasive, which signifies that its base has penetrated and is proliferating in the corium, it does in truth take on an apparent rapid increase in its rate of growth. Stryker's[21] description is explicit in remarking the zone of erythema and increase of thickness of keratoses that are progressing. Such a keratosis no longer loses nine-tenths of its mass each time the scale drops off. It seems to go into the cancer business suddenly and emphatically. It appears to have altered its basic nature and to have become a new thing. I believe the truth to be different, that no grave alteration has in fact occurred, and that the apparent jump in growth activity is explicable simply along the lines I have indicated. The "precancerosis" and the cancer evolved from it are one and the same thing seen at different times. The true rate of cellular division has not in fact changed, except that when ulceration occurs, inflammatory and loose tissue is available as a culture medium for tumor to grow into. The great-grandchildren of the original cancer cell are not different from the grandchildren. The malignancy has not altered a particle; the lesion is a cancer, was a cancer and will be the same cancer; the dividing line between precancer and cancer (a theoretical stumbling block of no mean proportions) does not exist, and the name should not be changed solely to satisfy an outworn hypothesis.

SUMMARY

The progress of development of the earliest recognizable cancerous lesion of the skin has been briefly outlined from clinical and histologic standpoints. The hypothesis of a one-cell origin of a skin cancer has been supported by and shown to accord with observation, because of the origin at a point, the centrifugal spread, and the habit of being first intra-epidermal and later invasive of the dermis. Argument is advanced that malignancy is basically a phenomenon of rate of growth; the apparent slow progress of the lesion until invasion of the corium occurs has been shown not necessarily to involve a change in rate of growth. Whitman's hypothesis of a one-cell origin in somatic mutation is a reasonable and fitting theory of the etiology of skin cancer.

REFERENCES

1. Whitman, R. C.: Jour. Cancer Research, **4**:181, April, 1919.
2. Hansemann D.: Virchow's Arch. f. path. Anat., **119**:229, Feb. 4, 1890.
3. Broders, A. C.: J.A.M.A., **99**:1670, Nov. 12, 1932.
4. Sutton, R. L., Jr.: Jour. Mo. State Med. Assn., **32**:224, June, 1935.
5. Molesworth, E. H.: Dermat. Wchnschr., **99**:945, July 21, 1934.
6. Findlay, G. M.: Lancet, p. 1229, June 7, 1930.
7. Roffo: J.A.M.A., **104**:1535, 1935.
8. Wood, F. C.: J.A.M.A., **84**:4.
9. Bowen, J. T.: Jour. Cutan. Dis., **30**:241, 1912.
10. Montgomery, H.: Arch. Dermat. & Syph., **20**:339, 1929.
11. Fraser, J. F.: Arch. Dermat. & Syph., **18**:809, Dec., 1928. Freudenthal, W.: Arch. f. Dermat. u. Syph., **152**:504, 1926. Jadassohn, J.: Beitrag. z. klin. Chir., **136**:345, 1926. Borst: Verhandl. d. deutsch. path. Gesellsch., **7**:118, 1904.
12. Ketron, L. W.: Jour. Cutan. Dis., **37**:22, 1919.
13. Mottram, J. C.: Amer. Jour. Cancer, **22**:801, 1934.
14. Franseen, C. C.; and Taylor, G. W.: Amer. Jour. Cancer Research, **20**:287, 1934.
15. Sutton, R. L., Jr.: J.A.M.A., **104**:433, Feb. 9, 1935.
16. Schmitz, H.; and Benjamin, E. L.: J.A.M.A., **103**:808, 1934.
17. Schmitz, H.; McJunkin, F. A.; and Macaluso, M. A.: Surg., Gyn. & Obst., **27**:337, March, 1934.
18. Eichenberg, H. E.: Ztschr. f. Geburtsh. u. Gyn., **111**:243, 1935.
19. Schmidt, M. B.: Die Verbreitungswege d. Carc., Jena, 1903.
20. Broders, A. C.: Arch. Surg., **11**:43, 1925; ibid: Med. Jour. & Record, **121**:133, 1925.
21. Stryker, G. V.: Jour. Mo. State Med. Assn., **30**:15, 1933.

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DISCUSSION (*Abstract*)

Dr. Garold V. Stryker, St. Louis, Mo.—I have followed with a great deal of interest the course of Dr. Sutton's thought in the matter of early, cutaneous carcinoma since his first paper in 1934. Though the existence of precancerosis has been doubted for a long time by many, it is Dr. Sutton to whom we owe thanks for having forcibly called attention to this glaring discrepancy in the terminology of dermatological lesions. The term "precancerous lesion" has little upon which to defend its existence, while the theory of somatic mutation which Dr. Sutton has proposed does for the most part fulfill those requisites which are necessary for its substantiation. If one accepts his theory, one must also accept with Whitman the belief that the earliest cancer is the earliest cell which, changed by mutation, retains the ability to reproduce without control of the host. This mutated cell as yet remains to be positively identified. This identification will no doubt be forthcoming when more attention is given the early lesions which have in the past been considered as simple keratoses. The theory of mutation of normal cells is not inconsistent with the present trend of thought on the etiology of cancer.

The acceptance of Dr. Sutton's conclusion presents another welcome solution. It would be possible in this way to eliminate from the already confused nomenclature of specific lesions the word "keratosis." There is not nor has there ever been except on the basis of admission of ignorance a reason for giving a Greek name to a pathological condition which in English could only be interpreted as an old person's horny excrescence.

The idea of a precancerous condition which was proposed almost forty years ago has been steadily losing cast as one lesion after another has been taken from this class and placed with true carcinoma. It was not long ago that Paget's disease of the nipple was considered a precancerous condition. There are few today who will arise to defend the lesion described by Bowen on the basis of a precancerous condition; in fact, it is doubtful that Bowen himself, in his original

study, felt that he was dealing with anything but carcinoma.

There are so many points of similarity in the pathological sections of Paget's disease, arsenical keratosis, senile keratosis and xeroderma pigmentosa, that it would not be consistent with good logic to consider them in any light other than that they are brothers under the skin.

AFRICAN SLEEPING SICKNESS: A CLINICAL STUDY*

By E. R. KELLERSBERGER, M.D.,
Bibanga, Congo Belge, Africa

Since 1916 it has been my privilege to be a medical missionary connected with the Southern Presbyterian Mission at Bibanga, in the Katanga Province of the Belgian Congo, central Africa. It fell to my lot to build up a medical practice from the beginning to the present small, poorly equipped, but well organized work. It is well-known that a medical missionary comes in contact with every kind of disease, in usually its worst form. This has been my experience, but by far the most important work has been done with trypanosomiasis, or the so-called African sleeping sickness.

Since 1924, when the present small hospital was completed, over 40,000 patients have been registered in this polyclinic. About 11,000 of them, or approximately 28 per cent, had sleeping sickness. Many of these patients came on foot from long distances and were controlled and housed in a camp made of grass huts or grass-covered, sun-dried brick structures, during their period of treatment. Others came from near-by villages once a week for their injections. Many cases were diagnosed after systematic examination of the whole population in each village at intervals of twice a year or oftener. This work was often done alone as "médecin agréé" of the Colony, or in cooperation with the medical services of the Colonial Government. In some villages the infection ran as high as 30 per cent in 1927, the peak year.

A very important fact is that most of the cases presented themselves voluntarily. About 75 per cent of all cases were observed for two years or more, and some for as long as five or ten years. The peak year (1927) furnished 2,915 new cases in a total of 35,545 examinations. More than 400 cases died at the hospital camp, either from sleeping sickness, usually in a tragically advanced stage, or from the ever present, intercurrent diseases, to which may be added semi-starvation. Another small group did not come regularly for treatment, while some left and did not return.

All cases can be divided roughly into three groups. The first group comprises those in apparent good health, with trypanosomes in the peripheral blood, with bouts of irregular fever, or persistent headaches, and inability to do full work. Such conditions abound in this land where everyone has malarial infection, and only the constant and routine examination of the blood by preferably a thick drop Giemsa preparation reveals these dangerous types of cases, which are the most active spreaders of the disease, especially since they infect clean tsetse flies. Whole families have succumbed in this manner, and there is reason to believe that in such cases the infection is frequently the result of mechanical transmission, especially by the omnipresent blood suckers, the mosquito, bedbugs, or lice, frequent in central Africa. Cases of this kind, in which it was possible to exclude outside infection, have been observed by us.

Under group two come those cases that present definite clinical symptoms, such as engorged and soft neck glands, constant headaches and irregular fever, tremors of hands and legs or tongue, slow, heavy speech, stupor and a generally retarded mental response. Such cases usually present that classical symptom of unconquerable stupor which gives the disease its name. A gland puncture usually demonstrates the parasite, while the lumbar puncture often reveals increased pressure, positive reaction for globulins and lymphocytic elements ranging as high as 2,000 cells per cubic millimeter. This group is the most important and numerous, comprising 75 per cent of our patients. It is not as dangerous as Group 1, the parasite being more rare in the blood stream. The patient is more difficult to cure, but is more easily controlled, as he is aware of his plight and seeks medical treatment.

Group 3 comprises all advanced cases, 13 per cent in our clinic, with varied symptoms, such as stuporous sleep, amounting at times almost to coma, incoordination of movements, occasionally involuntary defecation and urination, and sometimes a mild or violent insanity, of intermittent type. In such cases a lumbar puncture

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Fig. 1
Four advanced cases of sleeping sickness with typical facial expression.

is the best diagnostic as well as prognostic measure, the presence of the large so-called "muriform" type of cell described by Dr. Louise Pearce, of the Rockefeller Institute, being a bad sign. In our clinic, over 30,000 lumbar punctures have been done, mostly by the native nurses trained in our nurses' school.

Atoxyl, antimony, germanine and tryparsamide were the four drugs used. Atoxyl, used as "soamine," really the first drug to give any definitely beneficial results in sleeping sickness, was given a fair trial. The dose is as high as 1.00 gram maximum, once a week, intramuscularly. Six thousand eight hundred and sixty-one injections were given at Bibanga Clinic. A number of patients have been cured by this drug, some of whom have been observed for over seven years. The weak points of atoxyl are the danger of arsenical blindness, the need of a prolonged treatment, including several years of repeated series of injections, its uselessness in advanced cases, and the difficulty of persuading a native to submit to painful injections over a long period.

The antimony preparations have never been used alone in our experience, but always in conjunction with tryparsamide when there was a concomitant schistosomiasis, or when tryparsamide alone did not appear to be efficient. The dose is as high as 0.10 centigrams in a 1 per cent solution, intravenously. Antimony is a depressing drug. When used alone it seems less active than other preparations, and has been more successful in cattle trypanosomiasis, as demonstrated by Broden and others.

"Bayer 205," or germanine, was also largely used, over 4,000 injections being given intravenously, the average dose being 0.02 centigrams per kilogram of body weight. It is generally well supported and very small quantities (2 grams in one case of a woman) given in four doses of 0.50 centigram each, every three days, have cured early cases where the trypanosomes were essentially a blood parasite. On the contrary, all cases of the second or third group, even though showing marked temporary improvement, ended in relapse, and had to be shifted to tryparsamide. An ideal treatment, used more by the English observers than by the French or Belgians, is a combined therapy of germanine and tryparsamide.

The final and, at present, most useful drug for all cases is tryparsamide. Since 1924 this

Fig. 2
(Top) Characteristic stupor so often found in cases of sleeping sickness and ending in falling down in a heap.
(Bottom) Sleeping sickness with brain involved, going to sleep sitting up and falling down in a heap.

Fig. 3
Typical posture of advanced cases of sleeping sickness. They may lie this way for many hours.

has been the drug of choice in our clinic, and to date approximately 150,000 injections have been given by our native staff to 10,000 cases. After many studies the average dose has been put at 0.045 gram per kilogram of body weight. Anything in excess of this dose may cause blindness, especially in advanced cases, in which the patient is in poor condition, and therefore would support any drug poorly. To effect a cure the drug must be pressed to the limit of security. Each case must be considered individually, weighed and studied carefully as to its particular grouping. Concurrent diseases, especially malaria, hookworm, schistosomiasis or malnutrition, must be treated and nourishment given. Such treatment is ideal and is possible only in a hospital or well established center where an efficient and permanent staff is available. In itinerant work in the bush, where it is far more difficult to control the patient, who is often at the mercy of a poorly trained, unreliable native *"aide-infirmiere"* while the doctor or sanitary agent is elsewhere, it is certainly wiser to use smaller doses over longer periods. Hence the itinerant personnel of the Belgian Government never exceeds a 2-gram dose. However, the danger of creating artificial "arseno-resistant" cases exists under this regime. In accord with Dr. van den Branden, formerly *Chef Laboratoire* at Leopoldville, we believe that the much discussed true arseno-resistance is comparatively rare, and that some of the unfavorable cases, reported by other workers, notably Barlovatz, are due largely to insufficient dosage, or irregular administration, or factors not otherwise controlled. We suggest also that in unfavorable results the question of reinfection must be seriously considered, as well as the ever present intercurrent disease. It is self-evident that the patient who weighs 70 or more kilograms should receive more than the routine 2-gram weekly injection given to the average case weighing 40 kilograms. In our dispensary as much as 3 or even 4 grams are given to such a case per week, with fine results. Our experience has been that a series of 15 injections weekly is preferable to the 8 or 9 given formerly; and in cases where the central nervous system is involved, it is wiser to repeat the cure after a rest of from one to three months' time, depending upon the condition of the patient, after lumbar puncture and other examinations. The drug may be given continuously over long periods. We have given over 100 grams in a single series.

Tryparsamide as a rule cures cases of Group 1, but it is in the more advanced cases that it is the most efficient of all drugs, its most remarkable action being to render normal the spinal fluid, even where there are from 1-2000 lymphocytes per cubic millimeter in patients that are moribund and apparently hopelessly insane. Such hopeless cases have been cured, and these results have been controlled in many cases for six to seven years. It is essential to follow regular and energetic treatment and to control the patients for as long a time as possible, this method resembling very much the treatment for syphilis.

In 1927, we treated approximately 3,000 new cases, while in 1931, though we examined about the same number of cases in the same region, or *"rayon d'activite,"* we diagnosed only 835 cases, and in 1934 only 350 cases. This is very encouraging; but a constant reexamination of all the population, with an effort to control the movements of the people, especially at markets, springs, bathing places and river crossings and on long journeys, contributes to the stamping out of the disease.

Thanks to tryparsamide, it is possible to say

that human sleeping sickness is a curable disease, and that this scourge of central Africa is being checked and controlled by efficient examination and treatment of the populations. We consider as cured a case that is in good clinical condition one year after treatment and with negative laboratory examinations. As high as 75 per cent have been cured, and under the ideal conditions above mentioned it is possible to obtain an 80 or 90 per cent cure.

A search into literature on tropical medicine will reveal that the fight against sleeping sickness is being carried on more vigorously than ever, and it yet remains a great colonial problem, in which medical missionaries as well as government men and research workers here and abroad have a real share.

THE LIMITATIONS OF INTRAVENOUS UROGRAPHY*

By THOMAS D. MOORE, M.D.,
Memphis, Tennessee

Intravenous urography is widely employed as a diagnostic procedure not only by urologists, but by others whose chief interest lies in other branches of the profession. Very often it is depended upon solely and to the exclusion of other urological investigation. There is no denying that the information afforded by the intravenous urogram may be wholly adequate. It is also true that in many instances the information gained is incomplete and that additional data are necessary before a proper diagnosis can be made. Unless the limitations of the method are recognized and observed, errors in diagnosis and treatment frequently will occur. For instance, a patient was seen recently who complained of pain in the region of the left kidney; a roentgenologist had made an intravenous urogram and, although the left pyelogram appeared incompletely filled, he made a diagnosis of left renal tumor (*Fig. 1-A*). Because of this finding her home physician referred her to me. Cystoscopy and retrograde pyelography revealed a normal left kidney (*Fig. 1-B*). Further study of the case disclosed evidences of a tumor of the spinal cord which was later successfully removed, followed by complete relief of the pain in the region of the left kidney. Such an error in diagnosis may be explained in several ways: (1) inexperience in the interpretation of pyelograms; (2) unsatisfactory pyelograms for proper interpretation; (3) reluctance to request more complete data by employing the cystoscope with or without retrograde pyelography.

Intravenous urography has been used over a sufficiently long period that a true evaluation can be made of its merits. In the opinion of many, it has taken its place in the first rank of diagnostic measures; others are less enthusiastic of its value, who find it difficult to obtain pyelograms satisfactory for interpretation. Since it was introduced in 1929, it has undergone a number of improvements and refinements. The volume of fluid injected has been reduced from 100 to 20 c. c. and untoward reactions and pain along the course of the vein during injection have been all but eliminated. The high cost of the iodine compounds employed still acts as a deterrent from its wider use. Outside of the field of urology there is indisputable evidence that too much reliance is being placed upon intravenous urography, not only in studying the anatomical outline of the structures comprising the urinary tract, but as a renal functional test as well. It is time to pause and emphasize its shortcomings; at the same time, its advantages and indications may be stated. It behooves urologists to caution our friends among the roentgenologists, general diagnosticians and general surgeons not to depend too much upon this method of diagnosis. I have personal knowledge of a surgeon who has been known to explore a kidney which was not visualized in the intravenous urogram rather than request a cystoscopic investigation. It is common knowledge among urologists that lack of visualization in the urogram signifies permanently impaired or absent function in comparatively few instances; in fact, it may be stated without reservation that if the urogram discloses both kidneys of good function and normal outline, these findings may be conclusive, but the converse is not true. When there is failure of visualization in either renal area, before deciding that true absence of function exists, a complete urological investigation should be requested; poor or absent visualization should lead to consideration of the following possible factors: (1) temporary or reflex inhibition of function, such as commonly occurs in the presence of a ureteral calculus; (2) incomplete filling, rendering proper interpretation impossible; (3) hypersecretion and hypermotility with little or no media retained in the renal area; (4) non-calculus obstruction at the renal outlet or along the course of the ureter; if of

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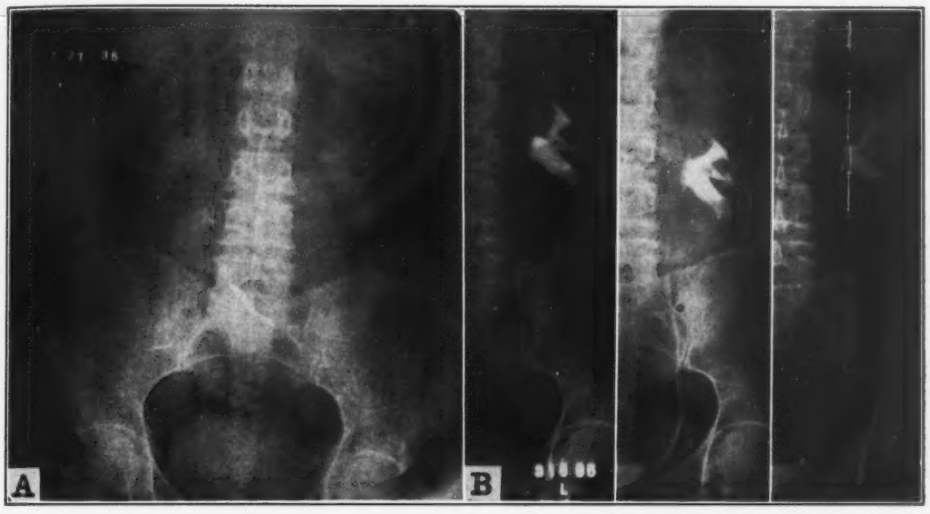

Fig. 1

(A) Intravenous urogram (made elsewhere); erroneous diagnosis of left renal tumor.

(B) Serial retrograde pyelograms proved that the left kidney was normal. Further study revealed evidence of a spinal cord tumor, removal of which was followed by relief of pain in the region of the left kidney.

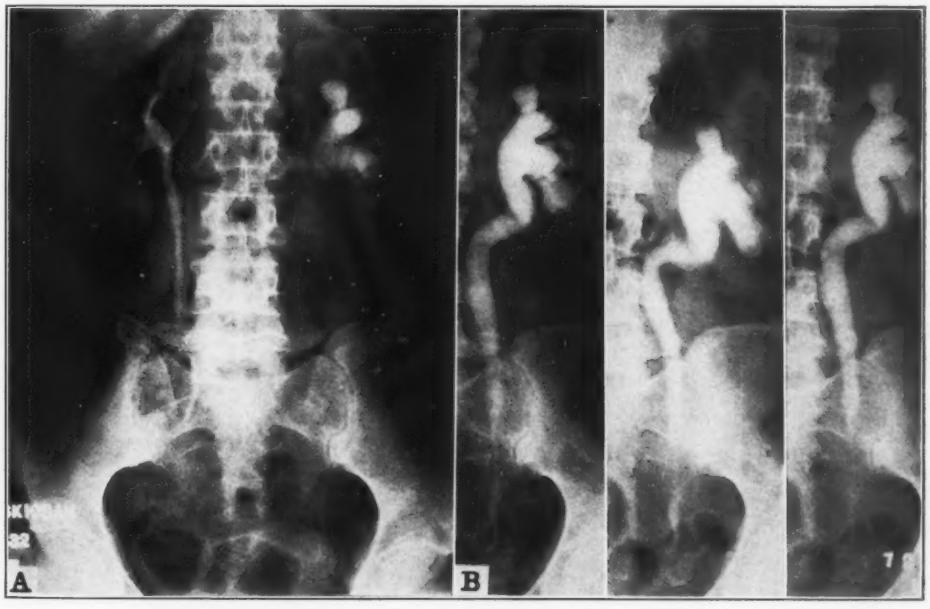

Fig. 2

(A) Intravenous urogram. Left pyelectasis and calicectasis with cause not apparent; therefore, cystoscopy indicated.

(B) Serial left retrograde pyelograms which clearly revealed the obstructive factor. Note the constant point of narrowing of the lower ureter with constant dilatation above, establishing the diagnosis of left ureteral stricture. Relieved by dilatations.

short duration, normal function will soon follow elimination of the obstruction; (5) temporary impairment of function due to nephritis and occasionally to toxic states; (6) true absence of function, such as may be caused by advanced renal tuberculosis, extensive neoplasm, or pyonephrosis. In consideration of these factors, who can state with assurance that a functionless or "dead kidney" exists on the evidence derived from the intravenous urogram alone?

Intravenous urography has been found most useful and dependable in the following conditions: (1) in the identification of doubtful shadows in the region of the upper urinary tract; (2) in the demonstration of renal and ureteral anomalies; (3) in proving or disproving the existence of stasis; (4) in the course of differential diagnosis, the observation that both kidneys are of normal outline and function often will render a cystoscopic examination unnecessary; (5) under circumstances in which instrumentation is inadvisable, such as acute specific urethritis, senility, patients in poor general condition, and in infants or small children. In the presence of gross hematuria or pyuria, in the majority of cases the information afforded by intravenous urography is inadequate for the determination of the cause or source of the blood or pus. The detection of renal tuberculosis in its early stage or the exclusion of this disease in the opposite kidney requires data other than that afforded by intravenous urography; the same may be said of the diagnosis of early neoplasms, which may cause slight deformities often not discernible in the urogram. Neither can the method be relied upon for the recognition of polycystic disease with its attendant poor function.

Good visualzation of the structures comprising the upper urinary tract will be greatly enhanced if due consideration is given technic. The following factors have been found of great importance: (1) the withholding of fluids for at least twelve hours prior to the examination, which induces a greater concentration of the media and therefore denser shadows; (2) a preliminary laxative for the elimination of intestinal markings; (3) of most importance is localized compression immediately above the symphysis pubis by placing a small rubber ball beneath the compression binder of the Potter-Bucky diaphragm, as previously advocated by the writer.[1] During the actual exposure of the films, the ball should be removed in order to permit the lower ureters to fill and to eliminate the shadow of the ball. This technic has been used with much satisfaction and often affords such good visualization of the ureters that doubtful shadows in the lower third may be readily identified and such lesions as strictures, kinks and dysfunction of the ureteral musculature may be studied, especially if serial films are obtained.

In an effort to gain an idea of the efficiency of intravenous urography, a critical review has

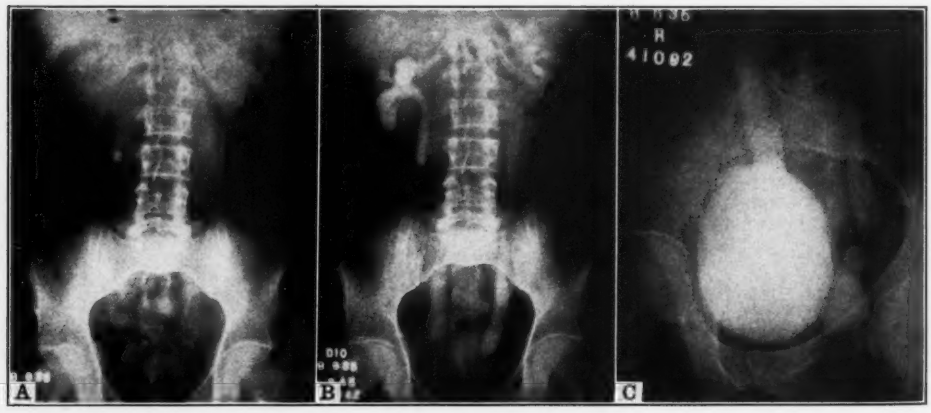

Fig. 3

(A) Plain roentgenogram. Gross hematuria and moderate urinary difficulty in a man of 32 years. Note suspicious shadow to right of third lumbar vertebra. In the region of the prostate gland was a small group of indefinite shadows.

(B) Intravenous urogram. Shadow included in upper right ureter with moderate secondary caliectasis. Bilateral hydroureters with cause not visualized in the urogram. Cystoscopy indicated.

(C) Cystoscopy and cystography disclosed a collar type of prostatic obstruction, with multiple prostatic calculi, and multiple diverticula of the bladder. Note that there is no evidence of the diverticula in the urogram (B).

been made of a group of one hundred fifty consecutive urograms obtained in my private practice. In the series only the latest improved media have been used (chiefly diodrast) with the patients routinely prepared and employing the technic herewith described. In ninety-seven, or approximately two-thirds the urogram alone sufficed. Of this number, in forty-nine the findings were negative. The most common indications for the examination of those with negative findings were as follows: (1) doubtful shadows in the regions of the kidneys or ureters; (2) pain suspected of having its origin in the upper urinary tract; (3) suspected urinary stasis, especially in cases of pyuria in juveniles, and in excluding hydronephrosis; (4) in a few instances palpable tumors in the lateral abdomen were proven to be extrarenal. Of the remaining forty-eight cases a positive urologic diagnosis was possible without the necessity of cystoscopic data (*Table 1*). It will be noted that the most common pathological condition in this group was calculous disease, of which there were sixteen cases involving the kidney and twelve of the ureter. This finding is in line with Braasch's[2] statement that

"The general use of urography will probably be limited to the recognition of hydronephrosis, the identifying of doubtful shadows, the estimate of renal function, and the demonstration of a normal pelvis."

In thirty-six cases a cystoscopic examination and retrograde pyelograms were made in addition to the intravenous urogram (*Table 2*). It

Table 1

A GROUP OF 97 PATIENTS IN WHICH INTRAVENOUS UROGRAPHY ALONE WAS SUFFICIENT FOR DIAGNOSIS

Lithiasis. renal	16
Lithiasis, ureteral	12
Anomalies	6
Hydronephrosis	5
Nephroptosis	3
Chronic pyelonephritis	2
Pyelitis of pregnancy	2
Renal neoplasm	1
Congenital renal deformity	1
Perinephric abscess	1
Chronic nephritis	1
Ureterocele	1
Ureteral stricture	1
Diagnosis NEGATIVE	49

Table 2

A GROUP OF 36 PATIENTS IN WHICH DIAGNOSIS REQUIRED CYSTOSCOPY AND RETROGRADE PYELOGRAPHY IN ADDITION TO INTRAVENOUS UROGRAPHY

Lithiasis, ureteral	10
Anomalies	5
Lithiasis, renal	3
Hydronephrosis	3
Renal neoplasm	3
Renal tuberculosis	3
Pyonephrosis	3
Essential hematuria	2
Pyelonephritis	2
Congenital solitary kidney	1
Ureteral stricture	1
Diagnosis NEGATIVE	6

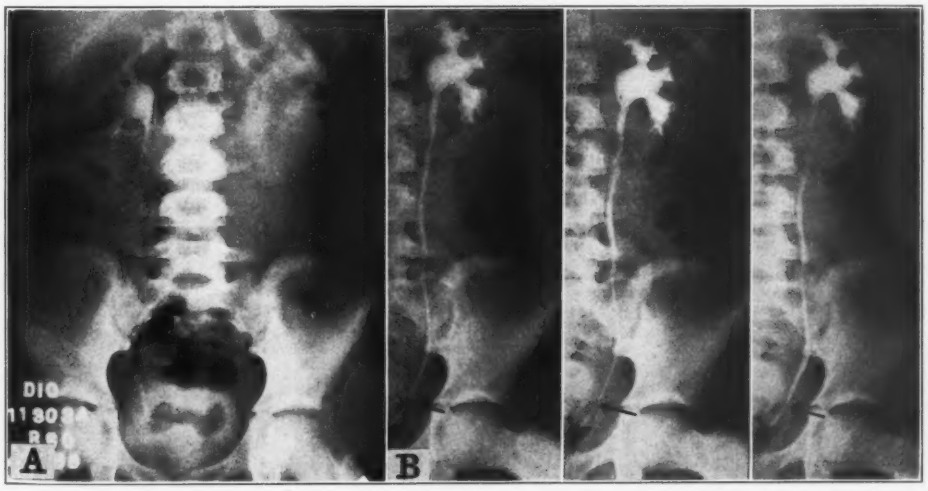

Fig. 4

(A) Intravenous urogram. Child of ten years complaining of severe pain in left loin. No evidence of left renal function with cause not apparent. Cystoscopy indicated.

(B) Serial left retrograde pyelograms. Note small constant filling defect in lower ureter produced by a stone which was permeable to the roentgen ray. Normal left renal function followed passage of the stone. Evidently an instance of reflex inhibition of function.

will be noted that there were negative findings in only six and that again lithiasis involving the kidney or ureter was the most common diagnosis. For many of these cases the urogram afforded a clue, such as a unilateral dysfunction or the evidence of pyelectasis with the underlying cause not apparent (*Fig. 2*). In none of this group was an accurate diagnosis possible without the information gained at the cystoscopic examination.

In a third group of seventeen cases (*Table 3*), cystoscopy was necessary, but without retrograde pyelography. It will be noted that lesions of the bladder and prostate were in the preponderance, often with secondary changes involving the upper urinary tract which were evident in the urogram (*Fig. 3*). It is also worthy of note that there were many instances in this group in which the urogram served to exclude the upper urinary tract in which a pathological condition involving the bladder, prostate or urethra was not revealed except by the subsequent cystoscopic study.

Table 3

A GROUP OF 17 PATIENTS IN WHICH DIAGNOSIS REQUIRED CYSTOSCOPY WITHOUT RETROGRADE PYELOGRAPHY IN ADDITION TO INTRAVENOUS UROGRAPHY

Neoplasm of bladder	4
Pyelonephritis	3
Lithiasis, ureteral	3
Prostatic obstruction	2
Lithiasis, renal	1
Hydronephrosis	1
Bilateral hydronephrosis, secondary to urethral stricture	1
Pyonephrosis	1
Essential hematuria	1
Diverticula of bladder	1
Multiple vesical calculi (x-ray permeable)	1
Contracted bladder	1
Diagnosis NEGATIVE	1

From a critical analysis of this limited series of urograms the following deductions seem reasonable: (1) intravenous urography serves admirably in the localization of doubtful shadows; in the demonstration of urinary stasis and anomalies; in the study of the urinary tract in children; in the pregnant state; in senility; and in demonstrating kidneys of normal outline and function. (2) In a group of one hundred fifty patients subjected to intravenous urography, approximately two-thirds required no further urological study, but in one-half of these the diagnosis was negative; the remaining third required cystoscopy with or without retrograde pyelography, revealing pathological conditions in all

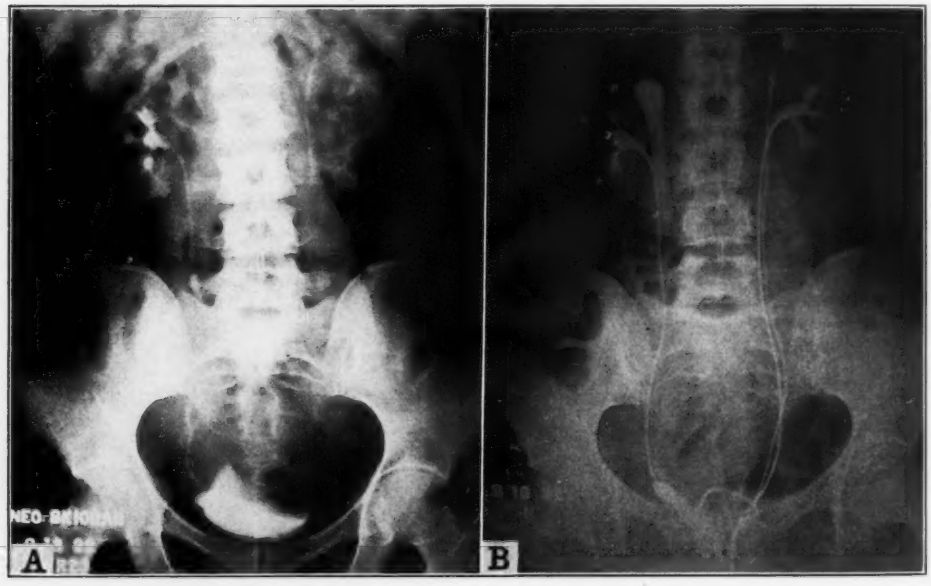

Fig. 5

(A) Intravenous urogram. Normal function and outline on the right side; left renal duplication with ureters not visualized. Urinary incontinence a symptom.

(B) Bilateral retrograde pyelograms. Note catheter coiled in a urethral diverticulum which receives an ectopic ureter originating from a functionless upper segment of a right renal duplication (completely missed by the intravenous urogram). Left renal and ureteral duplication also proven.

but seven, which the urogram had failed to completely disclose. (3) It is evident that lesions of the lower urinary tract will frequently be overlooked unless cystoscopy is employed. (4) The intravenous urogram often fails to reveal the underlying cause of urinary stasis; this should always be determined by a complete urological study and in most cases it is prerequisite to proper therapy. (5) Cystoscopy should be employed routinely before nephrectomy in renal tuberculosis in order to establish beyond question the status of the supposedly healthy kidney. (6) As a renal functional test intravenous urography can be relied upon if the function is normal; it is decidedly unreliable as an indicator of impaired or absent function. (7) In this series the urogram revealed unilateral absence of function in twenty-three instances, but in only ten of these was a truly functionless kidney found on cystoscopic examination. In eleven cases there were one or more stones in the ureter with temporary absence of function, proven by a return to normal following removal of the calculi. In two instances the media failed to appear in either renal area; in one there was an extensive malignancy of the bladder with partial occlusion of both ureters; in the other there was a horseshoe kidney with a functionless hydronephrosis of the right half and the left half was involved in a carcinoma complicated by a pyonephrosis.

A safe rule is never to depend on an intravenous urogram for the diagnosis of a functionless kidney. This finding should always demand a cystoscopic investigation and the dye tests for differential function. On the other hand, if the urogram portrays normal renal function, it may be relied upon; in my experience there has not been an instance of greatly impaired or absent function found at cystoscopy when the intravenous urogram revealed normal function. It may be said in conclusion that in common with many other diagnostic and laboratory procedures, intravenous urography is a test which is invaluable, but in most cases the information derived must be considered only as a part of the evidence. Proper interpretation must be correlated with the clinical and laboratory data and frequently a complete urologic study is imperative before an accurate diagnosis is possible. Urologists, with their background of experience in pyelographic diagnosis, will often be consulted in the interpretation of films made by those of lesser experience. They will do well to tactfully point out, when occasion demands, that the limitations of intravenous urography are indeed numerous, and unless constantly kept in mind, grievous errors in diagnosis and treatment will be inevitable.

REFERENCES

1. Moore, Thomas D.: Excretion Urography with Neoskiodan. Jour. Urol., **30**: No. 1, July, 1933.
2. Braasch, William F.: The Limitations of Intravenous Urography. Trans. Amer. Assn. Genito-Urinary Surgeons, pp. 109-114, 1931.

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DISCUSSION (*Abstract*)

Dr. J. Ullman Reaves, Mobile, Ala.—Excretory urography is the roentgenologic visualization of the urinary tract by the intravenous, oral, subcutaneous or rectal administration of substances that are radiopaque. It is quite fitting that our Association should have in its Urological Section a man who has been working diligently to interpret upper urinary pathology through urography. Such a man is Dr. Thomas D. Moore, of Memphis, and I wish to thank him for his remarks on excretory urography as evidenced here today.

The advantages of excretory urography have made it hard for us to justify a flat kidney-ureter-bladder roentgenogram. The men who are using excretory urography routinely find that it suffices in from 50 to 70 per cent of cases presented, being especially valuable in traumatic injuries of the upper urinary tract and in those cases in which the kidney function is nearly normal. It will not replace the catheter for the determination of the source of pus and blood nor will it eliminate retrograde instrumentation with urography where differentiation of kidney urine or function must be made. At first we thought that excretory urography would be a valuable kidney function test. It is valuable when the kidney function is normal or nearly normal, for it is upon the concentrating property of the kidney that the success of excretory urography depends. Therefore when the blood urea is high and the concentrating power of the kidney poor, the data obtained is negligible and the method is perhaps attended by more or less danger.

The technic outlined by Dr. Moore has been used by me for the past two and a half years, and I have attained better delineation of detail than others obtain with a different procedure. I have not perfect detail for interpretation when I use the compression ball, but this method is a great help toward obtaining perfect detail, despite Wesson and others to the contrary.

The finding of acid-fast bacilli in the catheterized urine is necessary to establish a diagnosis of tuberculosis. Unless there is advanced destruction of the kidney showing sharpness of outline in the urogram, why not rely upon retrograde pyelography where urine can be collected in order to diagnose these cases in their incipiency and estimate accurately the condition of the opposite kidney?

I wish to emphasize the point that excretory urogra-

phy is not to be relied upon in cases where it is essential to run a urinalysis on the kidney urines separately. More errors are caused by incomplete examination than from any other cause. When a patient presents symptoms which call for a urological survey, such a patient deserves a complete examination. Too many kidneys have already been removed because of an attempt to make a short-cut and eliminate the urologist and his complete kidney investigation. Bilateral and complete examination when proper methods are used is not, in most instances, dangerous or disturbing to the patient, and should be mandatory when the loss of a kidney is involved.

Too much emphasis cannot be made upon interpretation of the roentgenogram, for regardless of the method of urography employed, the patient fares best in the hands of the urologist or the roentgenologist who is trained in the proper interpretation of urological roentgenograms.

Dr. Edgar G. Ballenger, Atlanta, Ga.—Like many of our urologic papers, the important facts brought out by Dr. Moore need to be carried to the internist and surgeon even more than to the urologist, who is generally more conversant with the limitations of intravenous urography. While important facts and leads may be obtained without cystoscopic work, grave errors are likely to be made unless careful interpretations are made of intravenous urographic films. In fact, it probably requires greater experience in these interpretations than is required for cystoscopy.

The greatest advantage obtained by intravenous urography, where the diagnosis has not been cleared by this means, has been the lead which it gives as to what the next step should be. More orderly and more pertinent studies have thus been made possible.

Dr. Grayson Carroll, St. Louis, Mo.—The convincing clearness of this presentation makes us wish that all physicians in practice could hear it. It is manifestly the opinion, without controversy, of practically all urologists that intravenous urography has its limitations. Bransford Lewis succinctly states it as follows: "Intravenous urography is negative evidence when retrograde urography is positive evidence. It is invaluable in certain cases and extremely helpful in others, thus justifying a prominent place in diagnostic urology."

Considerable work has been done to determine the best procedure for obtaining satisfactory films. We find compression, with two small ovals in the pelvic region, is of assistance in concentrating the dye; also, dehydration for twenty-four hours prior to the injection is helpful. The gaseous distention of the bowel constitutes the major interference. The various methods of administrating the drug to absorb the gas or to expel it have not been universally worth while. Purgatives, enemas, given in various positions, etc., have likewise proven of no value. It is true that such cases having renal colic or other pain, influencing the sympathetic nervous system, will form gas despite any measure. For the undisturbed bowel no preparation whatsoever often proves the best.

THE TREATMENT OF TRAUMATIC ARTERIOVENOUS ANEURYSMS*

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Shortly after the beginning of the World War, Sir William Osler[1] delivered an address on arteriovenous aneurysms at Radcliff Infirmary, Oxford, in which he remarked that he had seen a greater number of these injuries after a few months' contact with war wounds than he had encountered in more than forty years of hospital practice.

He expressed surprise at the small number of specimens to be found in museums, and stated that the Royal College of Surgeons of England had only three, and that none were to be found in the Army Medical Museums.

In marked contrast to this, von Haberer,[2] a few years after the close of the war, in reviewing his experience as a military surgeon, stated that he himself had observed and treated 243 cases.

Of his limited observation of such injuries in private practice, Osler[1] said: "The truth is, England is not a country of brawls and dirks, and pistol wounds are rare in civil life."

One regrets that this cannot be said of America, where accidents incident to mechanized industry and rapid transportation, occasionally, and the reckless use of firearms and cutting weapons, very frequently, result in vascular injuries as serious and almost as numerous as those observed in time of war.

Stimulus imparted to the study of arteriovenous aneurysms by observations of large numbers of vascular wounds during and since the World War, has resulted, in the past twenty years, in the ascertainment of facts concerning these injuries not previously recognized; and the necessity for surgical intervention has been definitely established.

Chairman's Address, Section on Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

The most important revelation of these studies was the relationship of arteriovenous fistulae to cardiac enlargement and to the systemic effects which follow as signs of decompensation set in.

Gunnerman[3] in 1915, Caro[4] in 1916, Makins[5] in 1917, and Cazamian[6] in 1917, were among the earliest to suspect or recognize this relationship. In his 1915 address Osler[1] sensed it, but missed its full significance. He noted the intense venous engorgement in cases of long standing; and said of one patient whom he had followed for years and who finally succumbed to cardiac decompensation: "The condition of the heart may have had some connection with his long standing lesion."

When scientists realized that the claims for this relationship were well founded, the cardiac and systemic manifestations of arteriovenous aneurysms were subjected to exhaustive investigation by cardiologists, physiologists, physicists, as well as surgeons, with the result, as Matas[10] says, that "they have given the observation the character of an established fact."

In addition to the work of these earlier writers, Lewis and Drury,[7] in 1923, Hoover and Beams,[8] in 1924, and LaPlace,[9] in 1935, have contributed exhaustive reports from the cardiological standpoint. Conspicuous experimental work has been reported by Gage and Herrmann[15] and Barney Brooks,[16] in his Chairman's Address before the Section on Surgery of this Association in 1929, described fully and indicated graphically the changes in the circulatory mechanism brought about by an arteriovenous fistula and the alterations in the blood current following different types of ligation.

Outstanding surgical contributions in this country are those of Matas,[10] in 1923, in a paper delivered before the Southern Surgical Association "On the Systemic or Cardiovascular Effects of Arteriovenous Fistulae," and of Mont R. Reid, in 1931, in a paper before the same Association on "The Effect of Arteriovenous Aneurysms Upon the Heart."

In former years these wounds were rarely subjected to surgical attack; due, in part, to the stationary condition which many cases seem to reach, in part, to the then poorly developed technic in vascular surgery, and, in part, to a lack of knowledge of the cardiac sequelae of abnormal communications between arteries and veins of larger caliber.

Acceptance of the fact that an untreated arteriovenous aneurysm may lead to serious and perhaps fatal degenerative heart disease, and that closure of the fistula before the degenerative process has become too advanced will greatly improve if not entirely cure the heart lesion, stands as a pressing indication for timely operation upon injuries of this character.

PROGNOSIS

The location of the fistula and the size of the involved vessels influence the prognosis greatly. Matas[10] holds that "the larger the vessels and the closer the fistula to the heart, the sooner will decompensatory changes occur."

Reid[11] states that "It is generally true that those fistulae in the arms, neck and head are better tolerated than those in the lower extremity." Osler has made a similar observation. While these general rules may obtain, the severity of the peripheral symptoms in the right subclavian case reported by Gilcreest[18] in 1928, and of the cardiac symptoms in the left subclavian case reported by me[14] in 1932, lead me to look upon arteriovenous aneurysms of the neck as potentially the most serious in results and the most difficult from an operative standpoint which may be encountered.

Arteriovenous fistulae between vessels of the larger size are characterized by three groups of symptoms: local, peripheral, and central, cardiovascular or systemic. Briefly these are: locally, thrill, bruit and possibly a tumor; peripherally, edema, varicosities, ulceration, and perhaps gangrene; centrally, cardiovascular changes, which, in the main consist of dilatation of the artery proximal to the fistula; circulatory and blood pressure changes, hypertrophy and dilatation of the heart, and the development of a condition simulating aortic insufficiency. It is assumed that members of the audience are familiar with these groups of symptoms, hence they will not be further discussed at this time.

TREATMENT

The question of treatment depends upon the period at which the case comes under observation.

Immediate operation is seldom advisable, and the interval of delay before operation has been the subject of considerable difference of opinion. In discussing this feature, Reid says that, in the World War, the Germans operated in about three weeks, while the British and French waited for several months. Makins and Matas advise waiting two or three months, while Reid[12] believes

that cases should be held for six months following the injury.

Two cases of my series came under observation immediately after injury and were operated on the twenty-seventh and seventy-seventh days, respectively, with satisfactory results. The tissues were well healed and healthy and recovery was without infection. I am inclined to follow Matas and Makins and operate within two or three months.

Concerning the advantages of delay, Reid[12] has the following to say:

"In some cases, hemorrhage, increasing hematoma, infection, and, very rarely, acute cardiac symptoms make it necessary to operate soon after the injury. When none of the foregoing complications make operation imperative, delay presents the following advantages:

"(1) A good collateral circulation develops which permits excision of the fistula without the fear of gangrene.

"(2) The injured vessels become thoroughly healed, making their dissection easier and safer.

"(3) Infection is less likely to occur.

"(4) Spontaneous healing may take place."

From a consideration of the foregoing, it will be recognized that the method of approach will differ in dealing with a recent case from that employed in a late case.

In the early case, before arterial degeneration has taken place, the lumen of the main artery may be preserved by lateral suture, or possibly by end-to-end anastomosis. In a case of long standing this is seldom advisable, since the artery may be too much degenerated to make its restoration safe, and the collateral circulation, which quickly develops about arteriovenous fistulae, makes its preservation unnecessary. It is perhaps inadvisable in any case to attempt to preserve the lumen of the vein.

In recent cases more especially is it advisable to test the efficiency of the collateral circulation in an extremity before undertaking an operation which may require occlusion of the main arterial channel.

In long standing cases, where heart involvement is marked, Matas advises occlusion of the fistula by intermittent compression carried on over a considerable period of time in order to prepare the heart for the circulatory adjustment which will follow permanent closure of the fistula.

The underlying principle of every operative attack is to close definitely and permanently all abnormal communications between the arterial and venous systems. The method to be employed will depend upon the condition found at exploration.

The following methods have been successfully employed: ligation and division of a connecting channel; separation of artery and vein with restoration of each by suture; transvenous arterial suture; endo-aneurysmorrhaphy; quadruple ligation of main vessels and all tributaries, with excision of involved segments.

Proximal or proximal and distal ligation of arteries or veins has not proven successful and is no longer practiced.

Quadruple ligation and excision, while most formidable, and, in recent cases, least desirable, is often the only feasible method. In the groin, the elbow, and the neck, where large vessels give off numerous branches, it will be most often demanded. For example, the common femoral is an artery two inches long, giving off four large branches in its short course, and dividing into the superficial femoral and profunda. Any attempt to separate the vessels and preserve the artery will almost certainly be defeated by reason of hemorrhage from these branches and from smaller vessels which have become enlarged in the process of development of the collateral circulation.

Every effort must be made to obtain complete control over the circulation, by tourniquet, provisional ligatures or clamps, proximally and distally, on the venous as well as the arterial side, before any attempt is made to attack the site of the fistula, else severe hemorrhage will be encountered.

On account of the time which is required in dealing with complicated cases, local, regional and spinal anesthesia should be employed in preference to inhalation anesthetics wherever feasible. Cervical block and local infiltration have proven very satisfactory in operations upon the neck, and spinal anesthesia, followed, if necessary, by ether, has been used in operations upon the lower extremities. Silk is the suture material of preference, and the cases in this series with one exception have not been drained.

Since February, 1932, fourteen cases of traumatic arteriovenous aneurysms have come under my observation in my service at the Hillman Hospital and in the Employees' Hospital of the Tennessee Coal, Iron and Railroad Company, Fairfield, where, through the kindness of Dr. Lloyd Noland, Chief Surgeon, I have been called upon to operate upon those cases which have been admitted to that institution during this period.

The cases have been treated in collaboration with Dr. J. P. Collier, formerly resident surgeon at the Hillman Hospital, and with Dr. R. M. Pool, Chief of the Section on General Surgery at the Employees' Hospital.

LOCATION OF WOUNDS AND VESSELS INVOLVED

In the neck	2	Left external carotid and internal jugular	1
		Left subclavians	1
In the left chest	1	Left subclavians	1
At the bend of the elbow	2	Brachials	2
In the groin	4	Common femorals	4
In mid thigh	1	Superficial femorals	1
In the pelvis	1	External iliacs	1
Near ankle	1	Posterior tibials	1
In amputation stump lower third of leg	1	Posterior tibials	1
In cavernous sinus	1	Internal jugular cavernous sinus	1
	14		14

NATURE OF THE TRAUMA

Two cases resulted from industrial accidents: the pulsating exophthalmos followed a fall with fracture of the base of the skull, and the arteriovenous aneurysm in the amputation stump followed a crushing injury of the leg.

Of the remaining twelve, eight resulted from gunshot wounds and four followed incised or stab wounds.

RESULTS

Two patients have refused operation: left subclavian and right common femoral. Both have serious heart involvement and the femoral case is much inconvenienced by edema and varicose veins.

Two cases have recovered spontaneously: one femoral and one posterior tibial. The former recovered within a few weeks and the latter after several years.

One case, left brachial at elbow, is awaiting a favorable time for operation.

The pulsating exophthalmos is of seven years' standing, has improved considerably, and has not been definitely advised as to operation in view of the unsatisfactory results which have frequently followed operations on this particular lesion.

Of the eight cases subjected to operation, one patient died suddenly several hours after operation as a result of his long standing heart disease. In the left subclavian case, extreme cardiac decompensation was promptly arrested and the patient restored to comparatively active domestic usefulness. The others were definitely cured, though one died during convalescence from complicating disease.

CASE REPORTS

Case 1, Hillman Hospital No. 99626.—Arteriovenous aneurysm of the left external carotid artery and left internal jugular vein. Ligation and excision of vein. Arteriorrhaphy. Cure.

The patient sustained a gunshot wound of the left side of the face, involving the oral cavity, lower jaw and soft tissues of the left side of the neck. He was admitted to the Hillman Hospital July 5, 1935, 12 hours after being shot. A large hematoma filled the left side of the neck from mastoid to clavicle. The typical "machinery hum" bruit of an arteriovenous aneurysm was present.

The course of the bullet, the absence of cerebral symptoms which would have been expected in injury of the internal or common carotid artery, together with an almost imperceptible temporal pulse on the involved side, justified a diagnosis of arteriovenous fistula between the external carotid artery and the internal jugular vein. Hemorrhage had ceased and there was very little shock. Operation was postponed, awaiting subsidence of the hematoma and thorough healing of the wound, which, it should be remembered, involved the oral cavity. Five days after admission there was a moderate secondary hemorrhage from the wound in the mouth, but it soon ceased.

Within a few days, Branham's sign and the blood pressure phenomena could be elicited, but no cardiac symptoms developed. On August 1, 1935, twenty-seven days after the receipt of the injury, the hematoma having been absorbed and the wound being thoroughly healed, operation was carried out under cervical block anesthesia and local infiltration.

The operation presented some technical difficulties. It was found that the common carotid divided at an abnormally high level, and that the fistula was situated close to the base of the skull. After placing provisional ligatures upon the common carotid artery and the internal jugular vein proximal to the fistula, an attempt was made to expose the vessels above the fistula. While proceeding with great care, the vein was torn, and free hemorrhage from the artery as well as the vein took place. Tightening the proximal provisional ligatures controlled the bleeding from below, while clamps on the vein and digital compression of the external carotid artery controlled further bleeding until the artery could be closed by lateral sutures and the vein could be ligated above and below the fistula. Uninterrupted recovery resulted, and full restoration of the temporal pulse took place within a week.

Case 2, Hillman Hospital No. 64706.—Arteriovenous aneurysm left subclavian vessels, following stab wound of neck three years previously. Operation refused.

The patient was admitted to the hospital October 21, 1930, suffering from a stab wound above the left clavicle. He was treated for shock and remained in the hospital for nine days, when the wound had healed and he was discharged. No mention was made at that time of the presence of an arteriovenous fistula. He continued his work as a chauffeur and began to com-

Case 3, Fig. A

Site of the stab wound of the left chest. The point of penetration of the chest is at the upper end of the scar. The white dot indicates the point of greatest intensity of the thrill and bruit, and the white lines outline the area throughout which the bruit was audible.

plain, some months later, of dizziness and shortness of breath on exertion. About two years after the injury he was examined in another clinic and the presence of the arteriovenous aneurysm was discovered.

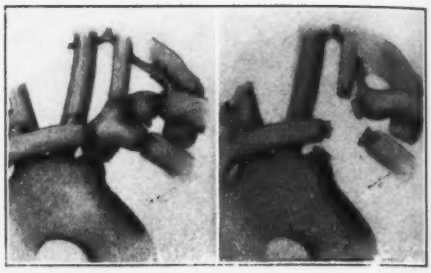
On examination at my office December 26, 1933, the typical local signs of arteriovenous aneurysm were present, also marked enlargement of the heart, with mitral and aortic blows. The location of the wound indicates that the fistulous communication is between the first portion of the subclavian artery and the adjacent vein.

Case 3, Hillman Hospital No. 72748.—Arteriovenous aneurysm of left subclavian vessels from stab wound of the chest in first interspace at left border of the sternum. Extreme cardiac decompensation developing within six weeks relieved by multiple ligation and excision in two-stage operation.

The case was reported in detail in the *American Journal of Surgery*, May, 1933.[14]

ARTERIOVENOUS ANEURYSMS OF RIGHT AND LEFT BRACHIAL VESSELS NEAR THE ELBOW (CASES 4 AND 5)

Case 4, white patient, entered Em-



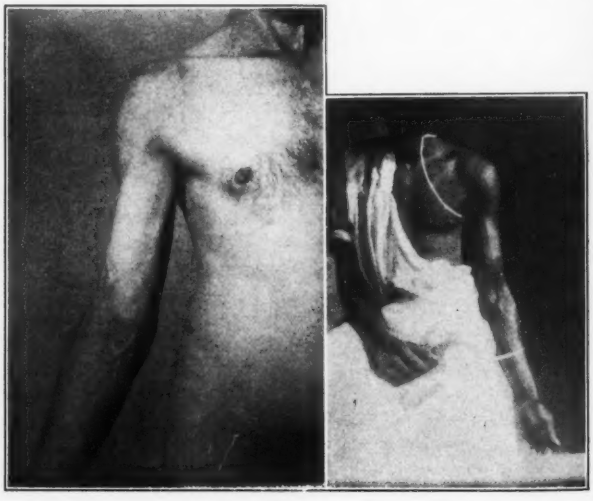
Case 3, Fig. B

The points of ligation and areas of excision of involved vessels (*from American Journey of Surgery*, reference 14).

ployees' Hospital November 17, 1934. Multiple ligations and excision. Cure.

Case 5, Hillman Hospital No. 92493.—Colored patient. Operation deferred.

The white patient received a gunshot wound of the arm 25 years previous to admission. His complaints were muscular weakness of the arm and coldness of the hand, making his work as a mechanic very difficult in cold weather. Though he had endured these discomforts for years, they were becoming progressively worse. The radial pulse was not perceptible. Branham's sign and blood pressure phenomena were not obtained and there were no cardiac changes. Operation consisted of multiple ligations and excision. Primary union fol-



A B

Cases 4 and 5, Figs. A and B

Case 4.—Note tumor at flexure of elbow and varicose veins; also markedly enlarged brachial artery and vein proximal to the site of the fistula.

Case 5.—This picture shows varicosities of arm, forearm, and at bend of elbow. The white lines around shoulder and forearm mark the area within which the bruit can be heard.

Case 4, Fig. C

Case 4.—This demonstrates the large size of the brachial artery and vein, and indicates the number of vessels which it was necessary to control by forceps and ligatures.

lowed, with immediate improvement in symptoms, with return of the radial pulse within ten days.

The colored patient sustained an incised wound near the elbow three years previous to this admission. At the time of the injury he had been treated for an incised wound and the arteriovenous fistula was overlooked, or had not developed. He refused operation on readmission on the ground that his work was not sufficiently interfered with to necessitate operation. He recently consulted me and requested operation, since the local symptoms were becoming more troublesome. He is awaiting a favorable time for returning to the hospital for operation.

Case 6, Hillman Hospital No. 73341.—Arteriovenous aneurysm of right common femoral vessels following stab wound of the groin. Quadruple ligation and excision. Cure.

Following a stab wound in March, 1931, a slowly developing gangrene of the leg resulted in amputation of the thigh in June, 1931, three months after receipt of the injury. He was treated in another city. He was admitted to the Hillman Hospital in February, 1932, on account of pain in the stump. Examination revealed an arteriovenous aneurysm with all the classical symptoms, including beginning cardiac enlargement.

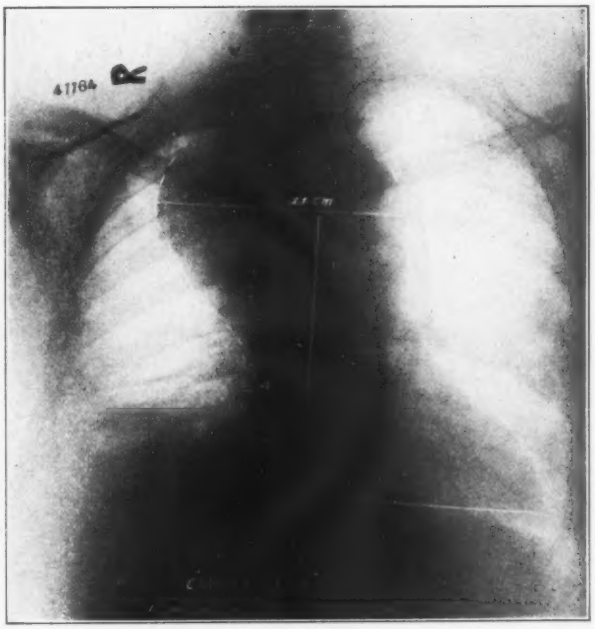
Quadruple ligation and excision were followed by complete cure.

This case presented the most serious peripheral disturbance which could follow such a vascular injury, namely, gangrene of the extremity. Since the gangrene was of slow development, amputation not being done for three months, one speculates as to what might have resulted from an earlier attack on the arteriovenous communication, after the manner of the German military surgeons. It might have been possible to restore the lumen of the artery by lateral suture, thereby preventing the gangrene and making the amputation unnecessary.

Case 7, Hillman Hospital No. 83413.—Traumatic arteriovenous aneurysm of the left common femoral vessels complicated by idiopathic aneurysm of innominate artery. Quadruple ligation and excision of arteriovenous aneurysm. Death during convalescence from rupture of innominate aneurysm.

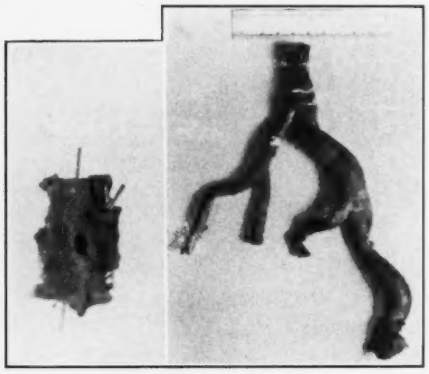
The patient was admitted with a diagnosis of thoracic aneurysm, and an arteriovenous aneurysm in the left groin was discovered in the course of the physical examination. This latter resulted from a gunshot wound sustained five years previously.

Examination of the chest revealed a pulsating tumor, without thrill or bruit, above the right clavicle. There was edema of the right upper extremity and the radial



Case 7, Fig. A

A.—X-ray of chest showing outline of thoracic aneurysm.



Case 7, Figs. B and C

B.—Arteriovenous fistula of left common femoral vessels. Specimen removed at operation.

C.—Postmortem specimen, lower end of aorta, right and left common, internal and external iliac arteries. The specimen demonstrates the enlargement of the artery which takes place proximal to the site of an arteriovenous fistula. It will be noted that the enlargement of the left common and external iliac arteries extends up to the aorta.

pulse was very weak. X-ray diagnosis was "aneurysm of innominate artery."

The left groin presented typical signs of an arteriovenous fistula, with peripheral and central signs.

A striking feature of the case was ascites, and in the month preceding operation repeated paracentesis was necessary, approximately 25,000 c. c. of fluid being withdrawn.

With such a complicated picture, one could not separate symptoms due to the arteriovenous fistula from those due to the innominate aneurysm. Since the innominate aneurysm seemed to be quiescent, we decided to operate upon the arteriovenous lesion with the hope of relieving some of his symptoms, and of being able, later, to relieve the pressure of his aneurysm by some sort of decompressive operation on the thoracic cage.

On August 20, under spinal anesthesia, quadruple ligation and excision of the arteriovenous aneurysm was carried out. Healing proceeded satisfactorily until the sixth day, when the innominate aneurysm ruptured and death took place two days later from slow leakage into the main bronchus of the right lung.

Autopsy revealed rupture of the aneurysm into the right lung. The aneurysm was filled with a firm clot; the first rib and clavicle were partly eroded; the endocardium presented no abnormalities; the liver was normal; there was no ascites.

The operative wound was healing by first intention; there was no impairment of the circulation of the extremity distal to the site of the fistula; the external and common iliac arteries of the involved side were much dilated, being approximately three times the size of the corresponding vessels of the opposite side; the external iliac artery contained a clot which extended from the point of ligation up to the bifurcation of the common iliac.

During the month previous to operation, paracentesis, practiced every few days, resulted in the withdrawal of several thousand c. c. of fluid. At autopsy the peritoneal cavity was free of ascitic fluid though paracentesis had not been employed for ten days before death, hence, it is probable that ascites, which had been a marked feature of this case, was due to the presence of the arteriovenous fistula.

Case 8, Hillman Hospital No. 72748.—Arteriovenous aneurysm of right common femoral vessels following gunshot wound nine years previously. Operation refused.

Swelling of the leg and cardiac symptoms were noted a few weeks after injury. Examination revealed: thrill, bruit, edema and varicose veins of the leg; mitral and aortic blows; Branham's sign and blood pressure phenomena are present, and teleroentgenogram shows an enlarged heart with 64.3 per cent cardio-thoracic ratio.

The patient would not submit to operation.

Case 9.—Arteriovenous aneurysm of right external iliac vessels, following gunshot wound of the loin ten months previously. Employees' Hospital, December, 1934. Quadruple ligation and excision. Cure.

The patient was shot February 2, 1934, remained in bed for two weeks, then resumed her household duties; noticed swelling in the leg within a few weeks; in July became conscious of a continuous "purring" in the right lower abdomen; was delivered of a full-term infant on October 19, eight months after the date of

Case 7, Fig. D

D.—Postmortem injection of vessels of the thighs and pelvis to demonstrate the vast network of enlarged vessels in left thigh about the site of the fistula. These provide an ample collateral circulation, so that excision of the fistula does not impair the integrity of the circulation of the extremity.

the injury. About November 1 she became bed-ridden on account of swelling of the right leg and thigh.

She was admitted to the Employees' Hospital in December, 1934, where examination revealed: thrill, widely transmitted bruit, edema of the entire right lower extremity and loss of the right patella reflex. The pulse rate was 110; the heart was enlarged to the left and a diastolic murmur was noted over the entire precordium. The fistula was not accessible to compression, hence Branham's bradicardiac phenomenon and blood pressure changes could not be elicited.

Operation was preceded by two weeks' rest in bed.

Operation, December 28, 1934, under spinal anesthesia, followed by ether, consisted of quadruple ligation, with excision of the involved area. At operation, when the fistula was closed, both the Branham sign and the blood pressure phenomena were demonsrated, the pulse rate falling from 100 to 64, and the blood pressure rising from 135/80 to 156/90. The recovery was uneventful, with slowing of the heart rate, reduction in its size, and rapid disappearance of the swelling of the thigh. The nutrition of the extremity was unimpaired.

At operation, the vessels were exposed extraperitoneally by a curved loin incision, such as is used for ureterectomy. With this incision we were able to expose and apply provisional ligatures to the external iliac vessels, proximally and distally, to the fistula. In the course of the operation bleeding from the external iliac vein was encountered, but it was easily controlled by digital compression until it could be secured by a ligature. There was a large venous sac, communicating with the artery by an opening 0.5 cm. in size. If the vessels had been more accessible, a transvenous arterial suture would have been possible. However, in the limitd space in which we were working the danger of

Case 9

This photograph shows marked swelling of the right lower extremity. The white dot on the right lower abdomen indicates the point of greatest intensity of the bruit; the circle indicates the area of thrill, and the white lines around the right foot, left leg and upper abdomen outline the wide area throughout which the bruit is audible.

Case 10

The dot on the end of the stump indicates the point of greatest intensity of the bruit, the line encircling the stump indicates the area of the thrill, and the line around the upper part of the thigh outlines the upper boundary of the area throughout which the bruit can be heard.

hemorrhage seemed too great to attempt this, and quadruple ligation and excision were deemed the safer procedures. The results were satisfactory in every way.

Attention is called to a similar case recently reported by Drs. Rienhoff and Hamman,[18] where excision of the fistula not only cured the arteriovenous aneurysm, but also cured a streptococcus blood stream infection. Vegetations were found on the margins of the fistulous communication.

Case 10.—Arteriovenous aneurysm of posterior tibials in an amputation stump, following crushing injury of the leg in 1925. Employees' Hospital, April, 1935. Endo-aneurysmorrhaphy. Cure.

This case is unique in my experience.

The patient has worn an artificial leg for ten years. On examination in March, 1935, an arteriovenous aneurysm, with typical thrill and machinery hum bruit, together with a large pulsating tumor, was found in the stump. Neither Branham's sign nor blood pressure changes would be elicited, but the circulatory apparatus was much disturbed, as indicated by a pulse rate of 110 while lying quietly in bed. This was perhaps independent of the arteriovenous aneurysm, as it did not improve after operation.

Endo-aneurysmorrhaphy was carried out under spinal anesthesia. The tumor was incised, clots and calcareous material were removed, three orifices were closed by suture, and the sac obliterated by plication. Examination showed that the sac was on the venous side, and that the artery adjacent was undilated. There was an uneventful recovery.

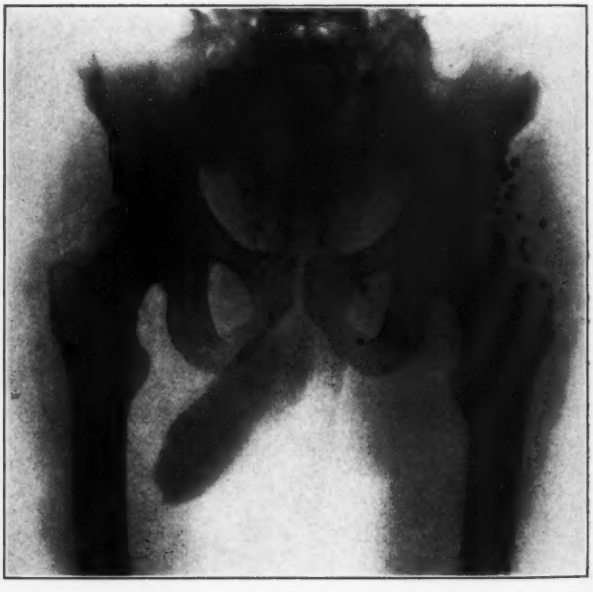
How shall one account for such a fistula? The most likely explanation is that a threaded needle was passed around a bleeding area, making a mass ligation; and that the needle perforated artery and vein, leaving a fistulous communication when healing took place.

Case 11, Hillman Hospital No. 79677.—Arteriovenous aneurysm of left femoral vessels at middle third of the thigh, following gunshot wound received nineteen years previous to admission. Quadruple ligation and excision. Death from sudden heart failure three hours after operation.

All the classical symptoms of arteriovenous aneurysm were present, and the history was that the patient had been shot in the thigh nineteen years previously. Especially to be noted were the varicosities and ulcerations of the leg, the harshness of the thrill, and the loudness and wide transmission of the bruit, as well as the enlargement of the heart and the simulation of aortic insufficiency.

Case 11

Photograph shows varicose veins and partly healed ulcer of leg, typical of arteriovenous aneurysm of femoral vessels of long standing.



Case 13

X-ray of pelvis showing numerous small shot in the region of the hip joint and along the course of the femoral vessels. Spontaneous recovery took place within a few weeks.

The operation was technically simple, and his sudden death a few hours after its completion indicated that the heart was not properly prepared for the readjustment of the circulation following the closure of the fistula. Prolonged intermittent compression of the fistula previous to operation, as advised by Matas, would probably have been followed by a different outcome.

Case 12.—Pulsating exophthalmos from fracture of the base of the skull following a fall seven years previously. Employees' Hospital.

In November, 1928, this patient fell and sustained a fracture of the base of the skull. Within 48 hours he complained of roaring in his left ear, and within four days a bruit and exophthalmos were noted. He received only expectant treatment and lost the sight of the left eye.

Seven years after the injury he presents a thrill and bruit, exophthalmos and a pulsating tumor over the inner canthus, and is practically blind in the left eye. The roaring in the ear is much less troublesome than formerly, and he feels better.

Since he has already lost the sight of the eye, and is suffering less than formerly from the noises in the head, it is doubtful that surgery is specially indicated. Attention is called to an operation devised by Dandy[17] and practiced by him in two instances, where, after failure to cure by proximal ligation of the internal carotid artery, he has turned down a bone flap and occluded the artery by a silver clip after it has emerged from the cavernous sinus.

SPONTANEOUS RECOVERIES

Case 13, Hillman Hospital No. 84108.—Arteriovenous fistula of the left common femoral vessels, following gunshot wound of the groin. Spontaneous recovery.

On August 11, 1933, the patient sustained gunshot wounds of the left forearm and left thigh. Compound fractures of both bones of the forearm resulted, but the wounds in the thigh involved only the soft parts.

Ten days after admission, the thrill and bruit of an arteriovenous fistula were noted in the left groin. Neither Branham's sign nor blood pressure changes could be elicited, indicating that the fistula was small. While awaiting a suitable time for operation, the signs of arteriovenous fistula became less marked, and on his discharge from the hospital on the thirty-eighth day after injury they were scarcely to be detected. He was observed from time to time in the clinic and made a complete spontaneous recovery.

Case 14.—Arteriovenous aneurysm of the posterior tibial vessels following gunshot wound in the right leg two inches above the ankle twelve years ago. Spontaneous recovery.

Patient came under my care at St. Vincent's Hospital immediately after injury and refused operation. Numerous examinations of the patient were made over a period of several years, each one showing that the fistula was still present. I recently looked him up for the purpose of reporting the case and found that the fistula had completely healed. The site of the former communication is represented by a scar and a firm nonpulsating tumor approximately 2 cm. in diameter.

REFERENCES

1. Osler, Sir William: Arteriovenous Aneurysms. The Lancet, London, **1**:949-955, May 8, 1915.
2. Haberer, H.: Aneurysms Interesting from Clinical and Operative Viewpoints. Deutsche Ltschr. f. Chir., **196**:215-19, 1926.
3. Gundermann, W.: Kriegschirurgist Bericht aur d. Geissener Klinik. Bruns' Beitrage, Bd., **97**:479, 1915.
4. Caro: Blutdrucksteigerung und pulsversamgsamung bei Kompression Traumatischer Aneurysmen. Mitt. a. d. Grenzgeb. und Chir., Bd., 29. Heft 3, S. 355, 1916.
5. Makins, Sir G. H.: On the Effects upon the Heart and General Circulation which Follow Wounds of the Blood Vessels and on the Variation in the Local Physical Signs Present at the Site of Injury. Brit. Jour. Surg., **4**:531, 1916-17.
6. Cazamian: Quelques Considerations sur le Retentissement Cardiaque et Circulatoire d'un Aneurisme Arteriovenaux d'Origine Traumatique des Vaisseoux. Bull. et mem. Soc. Med. d. hop. de Paris, p. 46, 12 Janview, 1917.
7. Lewis, T.; and Drury, A. M.: Observations Relating to Arteriovenous Aneurysms: Clinical and Experimental. Heart, London, **10**:301-389, 1923.
8. Hoover, C. F.; and Beams, A. J.: The Diagnosis and Pathological Physiology of Arteriovenous Aneurysms. Arch. Int. Med., **33**:1-22, 1924.
9. La Place, L. B.: Effect of An Arteriovenous Fistula on the Human Circulation. Amer. Jour. Med. Sci., April, 1935.
10. Matas, R.: On the Systemic or Cardiovascular Effects of Arteriovenous Fistulae. Trans. Sou. Surg. Assn., **36**:623-681, 1923.
11. Reid, Mont. R.: Effect of Arteriovenous Aneurysms upon the Heart. Trans. Sou. Surg. Assn., **44**:356-371, 1931.
12. Reid, Mont. R.: Abnormal Arteriovenous Communications, Acquired and Congenital. Arch. Surg., **11**:237-254, 1925.
13. Gilcreest, Edgar L.: Traumatic Arteriovenous Subclavian Aneurysm. Trans. Sou. Surg. Assn., **41**:188-210, 1928.
14. Mason, J. M.: Extreme Cardiac Decompensation Following Traumatic Arteriovenous Fistula of the Left Subclavian Vessels. Amer. Jour. Surg., **20**:451-473, May, 1933.
15. Gage, M. B.; and Herrmann, George: Observations on Experimental Arteriovenous Aneurysm. Proc. Soc. Exper. Biol. & Med., **25**:765, 1928.
16. Brooks, Barney: The Treatment of Traumatic Arteriovenous Aneurysms. Sou. Med. Jour., **23**:100-106 (Feb.) 1930.
17. Dandy, Walter E.: The Treatment of Carotid Cavernous Arteriovenous Aneurysms. Ann. Surg., **102**:916-927 (Nov.) 1935.
18. Rienhoff, W. F., Jr.; and Hamman, Louis: Subacute Streptococcus Viridans Septicemia. Ann. Surg., **102**:905-16 (Nov.) 1935.

WANDERING BULLET IN THE SPINAL CANAL: REPORT OF A CASE*

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The literature, particularly in times of war, abounds in case reports, and clinical, pathological, physiological and statistical studies of gunshot wounds of the vertebrae and spinal cord. It is an interesting fact that the first operations for lesion of the spinal cord ever performed were done by Géraud[1] and Louis[2] in 1750 and 1792, respectively, for gunshot wounds, nearly a hundred years before Horsley's[3] famous lam-

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inectomy for tumor.* Even in the early period when vertebral surgery for fracture, for Pott's disease and for tumor was being condemned as useless and barbarous (the details of this controversy were set forth with great faithfulness in the series of papers by Chipault[4 5 6 7 8] and the lengthy reviews of White[9] and Lloyd[10]), many writers were urging that most gunshot wounds of the spinal cord be operated upon (Vincent,[11] Prewitt,[12] Alessandri and Mingazzini[13]).

With the rapid development of neurological surgery in the past thirty years, the operation of laminectomy has become standardized and recognized as a relatively simple, though arduous procedure. The experience of the World War led to a general consensus of opinion that gunshot wounds of the spinal cord, particularly those in which the cord was compressed by missiles, fragments of bone or blood clot, should be treated by early and radical operation, with removal of all foreign bodies from the spinal canal. Notable among the numerous papers on the subject are those of Frazier,[14] Craig,[15] Hull,[16] Krause,[17] Symonds,[18] Holmes[19] and Mauclaire.[20 21]

The majority of spinal wounds occur in the dorsal and upper lumbar regions. Wounds of the cervical cord are less common and those of the cauda equina are quite rare. Hassin, Johnstone and Carr,[22] in 1916, could find only ten cases of cauda equina wounds in the literature (in addition to which they reported a case of their own), but such lesions are undoubtedly more common than this number indicates. For example, Cumston,[23] in 1919, reported twenty-two wounds of the cauda equina in a total of 225 spinal wounds seen in a single hospital.

That metallic foreign bodies may change their positions in both the brain and spinal canal has long been known, although it is rarely mentioned in the literature. Spontaneous movements of bullets in the brain were observed experimentally by Flourens[24] in 1862 and clinical cases of so-called "wandering bullet" in the brain have been reported by Regard,[25] Enderlen,[26] Vilvandré and Morgan,[27] Weaver[28] and others.† In the brain, these heavy foreign bodies move by virtue of their own weight through the soft brain substance, but in the spinal canal movement of a foreign body is possible because of the relatively large space (filled, of course, with cerebrospinal fluid) between the cord or cauda equina and the dura mater.

In 1891, Mudd[30] reported a case in which a bullet entered the spinal canal at the level of the eleventh dorsal vertebra. At operation it could not be found, but at autopsy it was discovered in the canal "three or four vertebrae below the point of entrance." In 1893, Pyle[31] removed a piece of a bullet which lay "loose in the canal." Loison,[32] in 1901, reported the use of stereoscopic x-rays in the location of a bullet which dropped in the spinal canal from between the first and second lumbar vertebrae to the level of the second sacral. It was finally removed at the third operation. Similar cases in which the bullets have moved downward in the canal have been reported by Mauclaire,[20] Tuffier,[33] Auvray[34] and Bulkley and Bergamini.[35] In only two instances, reported by Selberg[36] and Roberts,[37] respectively, have the bullets moved upward in the canal. Mauclaire,[21] in 1921, called attention to the fact that bullets in the spinal canal change their positions, but he reported no new cases.

REPORT OF A CASE

S. M. (V. U. H. No. 66116; referred by Dr. J. O. Walker, of Franklin, Tennessee), a 16-year-old boy, was admitted to the Vanderbilt University Hospital on September 8, 1934, two hours after having been shot in the abdomen from a distance of five feet by a .22 caliber automatic pistol. When the pistol was discharged, he experienced no abdominal pain and did not fall, but immediately began to have intermittent severe "shooting" pain down the back of his right thigh and leg. He was taken to his family physician, who gave him 0.015 gram of morphia and 0.0004 gram of atropine hypodermically and sent him at once to the hospital. He remained drowsy during the twenty-mile trip, but did not lose consciousness and complained of occasional cramping abdominal pains and of continued sharp pain in the right leg. He vomited once and soiled his clothes with urine and feces. Subsequent questioning revealed no significant facts in his past or family histories.

When admitted to the hospital, he was in a state of shock. The skin and mucous membranes were pale, the extremities were cold, he was sweating freely, the pulse was rapid and feeble and the blood pressure was 60 systolic and 42 diastolic. He could be aroused with difficulty and was somewhat irrational. The respirations were rapid. There was no cough and the lungs were clear to examination. In the midline of the epigastrium, 10 cm. below the xiphoid process was a bullet hole which did not bleed. The abdomen was generally tender and there was moderate generalized abdominal rigidity, but no distention. There was no wound of exit. The patient's condition did not permit complete neurological examination, but it was apparent that there was marked sensory and motor impairment in the right lower extremity. He did not move it spontaneously

*According to Chipault,[4] de Bazy performed a laminectomy for tumor in December, 1886, ten months before Horsley's operation.

†I have recently reviewed the literature on the subject of penetrating wounds of the brain in another paper.[29]

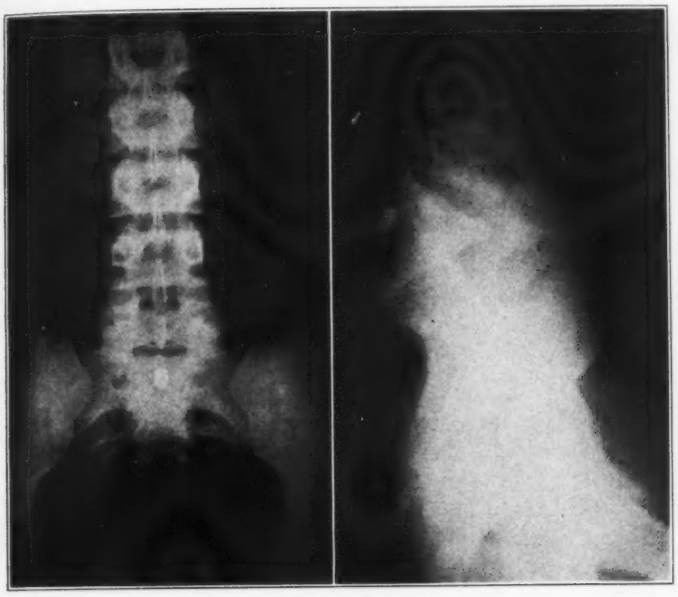

Fig. 1
Roentgenograms made on admission. The bullet lies in the spinal canal opposite the first sacral segment.

and did not respond to painful stimuli in the right leg. The knee-jerk and ankle-jerk could not be obtained on the right, but were present on the left, and he could move the left lower extremity normally.

It was apparent that the patient was having profuse intra-abdominal hemorrhage and he was prepared for operation immediately. While the operating room was being prepared, antero-posterior and lateral roentgenograms were made of the entire spine. These showed the bullet apparently in the spinal canal at the level of the first sacral segment (*Fig. 1*). There was no fracture and the bullet tract was not visualized, so that it was impossible to determine how or where it entered the canal.

The patient was given 700 c. c. of blood by direct transfusion with considerable improvement in his condition and laparotomy was performed at once by Dr. R. M. Larsen.

First Operation: Laparotomy and Closure of a Bleeding Wound in the Pancreas; Ether Anesthesia.—The long incision extended from the xiphoid to the symphysis pubis. Approximately 1,500 c. c. of blood were rapidly removed from the peritoneal cavity. A bullet hole was found in the gastrocolic ligament and this structure was divided, opening the lesser omental sac. The bullet was found to have passed through the mid-portion of the pancreas, which was bleeding profusely. The hole in its anterior surface was closed with catgut stitches and when this was done all bleeding ceased. A small partial perforation near the lesser curvature of the stomach was also closed. No other injury of the abdominal viscera or of the great vessels could be found. A huge retroperitoneal hematoma extended from the level of the pancreas along the spine on both sides into the pelvis. The wound was closed and the patient again transfused.

The patient's postoperative course was quite stormy. He was wildly delirious for three days, had irrational periods for several days thereafter. The temperature remained elevated (101 to 103° F.), he had considerable abdominal distention and complete retention of urine, requiring the insertion of an indwelling catheter. He was given nothing by mouth for five days, fluids being given by hypodermoclysis. At no time did signs of meningeal irritation occur. He was given 23,000 units of tetanus antitoxin in divided doses.

As soon as the patient was completely rational, neurological examination was performed. On the right side, there was diminished tactile, painful and temperature sensation throughout the entire distribution of the sacral nerves, progressively more marked from the upper to the lower sacral segments. On the left side, a much less marked impairment of all forms of sensation was present in the same distribution (*Fig. 2*). There was no demonstrable impairment of sensory function in the lumbar cord or nerves. There was marked weakness of the right anterior tibial muscle group and of all muscles of the right foot and moderate weakness of all other muscles inserted below the right knee. No definite motor weakness could be demonstrated on the

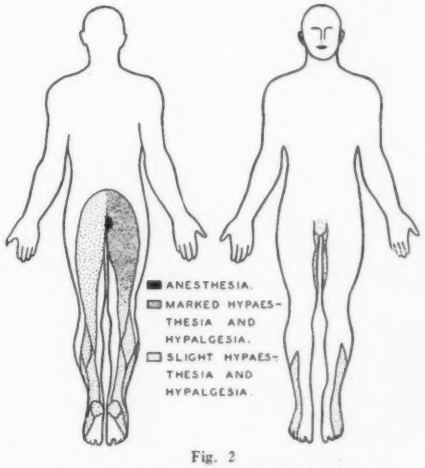

Fig. 2
Sensory chart preceding first laminectomy.

Fig. 3

Roentgenograms made following the first spinal exploration. The bullet lies between the fourth and fifth lumbar vertebrae. Note the silver clips which mark the ends of the dural incision.

left. The anal sphincter was relaxed. The right knee-jerk and ankle-jerk were still absent. No spasticity, clonus or abnormal toe responses were present. Lumbar puncture elicited clear, colorless cerebrospinal fluid under normal pressure, containing forty-nine polymorphonuclear leukocytes but no bacteria on smear or culture. There were prompt, normal responses to jugular compression and release.

Removal of the bullet was advised and, when the patient's condition finally permitted, laminectomy was performed.

Second Operation: October 4, 1934. Lumbar Laminectomy.—The bullet was not found. Under ether anesthesia, a midline incision was made and wide laminectomy done from the fourth lumbar vertebra to the third sacral segment, inclusive. The soft tissues and bone showed no evidence of injury. The dura appeared normal except for a small area of constriction and slight discoloration in the lower portion of the wound. The dura was opened and at the constricted spot seemed indurated and somewhat contracted, but the nerves of the cauda equina appeared normal. The cerebrospinal fluid was colorless and flowed freely. The bullet was not visible. A careful search was made both intradurally and extradurally without finding it. A small soft rubber catheter was inserted upward inside the dura for a distance of 20 cm. without meeting the slightest obstruction. Below, the end of the dural cul-de-sac was clearly visible. Silver clips were placed at the upper and lower ends of the dural incision as landmarks for future roentgenography and the dura and remainder of the wound closed in layers with interrupted silk stitches after the muscles were drawn together with silver wire.

The patient's postoperative recovery was rapid and uneventful. There was a definite but slight improvement in both the motor and sensory functions. The tendon reflexes in the right leg returned, but remained sluggish. The urinary retention persisted as before. On the sixth day after operation, roentgenograms showed the bullet lying at the level of the upper border of the fourth lumbar vertebrae, just above the upper silver clip (*Fig. 3*).

Third Operation: October 15, 1934.—Manipulation under the fluoroscope, re-exploration of the lumbosacral canal and removal of the bullet. The patient was placed on the fluoroscopic table, the head of the table elevated to a thirty degree angle and the patient's body vigorously shaken. The bullet immediately dropped to the level of the middle of the old wound. With the upper part of his body kept carefully elevated, he was taken to the operating room and the laminectomy wound reopened under local anesthesia (a small amount of nitrous oxide was given when the dura was exposed). A dark, bulging spot on the dura in the middle of the wound disclosed the location of the bullet. A small opening was made in the dura. The bullet, a copper jacketed .22 short, slightly dented on one side (*Fig. 4*) lay free among the roots

Fig. 4

Photograph of the bullet.

of the cauda equina. It was removed without difficulty and the wound closed as before.

His postoperative course was again satisfactory. The wound healed rapidly. The neurological functions gradually improved. Ten days after operation sensation was normal on the left and only slightly diminished in the right sacral distribution (*Fig. 5*). He could move his right toes fairly well and all the right leg muscles had gained strength. The knee-jerk and ankle-jerk were normal. Urinary retention persisted and, in spite of frequent bladder irrigations, he finally got a urinary infection. It was thought wiser to give him suprapubic bladder drainage.

Fourth Operation: October 29, 1934.—Suprapubic

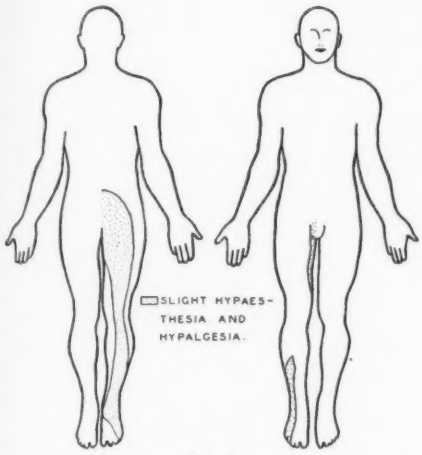

Fig. 5
Sensory chart shortly before discharge from the hospital.

cystostomy by Dr. E. H. Barksdale. Under nitrous oxide anesthesia, a No. 30 F. mushroom catheter was inserted into the bladder through a short suprapubic incision.

The infection subsided and the patient was discharged from the hospital on November 3, 1934.

He was seen regularly in the Out-Patient Department. On November 10, 1934, he was passing urine involuntarily through his urethra. On December 4, 1934, he could walk with the aid of crutches, but still had a marked foot-drop on the right. On December 8, 1934, he returned with acute pyelitis after having had chills and fever for six days. He was readmitted to the hospital for six days, during which the infection cleared up satisfactorily. At this time there remained slight hypesthesia and hypalgesia in the sacral distribution on the right. The weak muscle groups all showed definite improvement. Reflexes were normal. There was no spasticity. On February 2, 1935, he had regained voluntary control of urination, though there was still some leakage through the suprapubic sinus, and on February 28, 1935, he had begun to walk without crutches. From that time, improvement continued progressively. The suprapubic sinus closed, strength returned in the weak muscles and sensation returned to normal. When he was last seen, on September 1, 1935, the only abnormal neurological finding was an almost imperceptible weakness of the right tibialis anterior muscle. A mild cystitis was still present.

COMMENT

This case is of particular interest for several reasons:

First, it is remarkable that the bullet should have entered the spinal canal from the anterior side, reaching the free space in the canal posterior to the cord or cauda equina without having done more damage to these structures or to the bones of the vertebral column. In nearly all such cases, the bone has been shattered or the cord completely severed or both. Potherat[88] reported the only similar case, but in his patient the bullet lay extradurally anterior to the cord and the patient had paraplegia and anesthesia below the level of the bullet (between the eleventh and twelfth dorsal vertebrae).

Secondly, the question arises as to whether the nerve injuries in this case were actually due to the bullet or whether they may not have resulted from compression of the nerves by a large hematoma lying anterior to the spine. The only analogous case found in the literature is that reported by Fergor,[89] whose patient had a bullet in the spinal canal at the upper lumbar level without any neurological symptoms whatever. The bullet was not removed and the case was followed only a short time. Regardless of whether the bullet was the direct cause of the nerve injury in the present case, it is certain that it would sooner or later have caused trouble and that its removal was wise.

Thirdly, the bullet in the present case is known to have moved freely both up and down the spinal canal and its position could be changed at will by altering the position of the patient's body. It seems likely that it was pushed ahead of the exploratory catheter at the time of the first spinal exploration. The case serves as a pointed warning that the exact position of foreign bodies thought to be in the spinal canal should be determined immediately before the exploration for their removal.

BIBLIOGRAPHY

1. Geraud: cited by Chipault, ref. no 5.
2. Louis: Arch. gen. de Med., **2**:417, 1836. Cited by Chipault, ref. nos. 4 and 5, and by White, ref. no. 9.
3. Gowers, W. R.; and Horsley, V.: A Case of Tumor of the Spinal Cord: Removal, Recovery. Trans. Med. chir. Soc., London, **71**:377, 1888.
The report is also abstracted in the Brit. Med. Jour., **1**: 1273, 1888.
4. Chipault, A.: Chirurgie de la moelle et des racines medullaires. Rev. de Chir., **12**:685, 1892.
5. Ibid, **13**:201, 1893.
6. Ibid: De la trepanation rachidienne. Gaz. de Hop., **63**: 809, 1890.
7. Ibid: p. 969.
8. Ibid: p. 981. See also Arch. gen. de Med., **2**:444, 560 and 676, 1890.
9. White, J. W.: The Surgery of the Spine. Therp. Gaz., **15**: 656, 1893. See also ref. no. 30.
10. Lloyd, S.: Laminectomy: A Review of One Hundred and Three Cases of Spinal Surgery. Amer. Jour. Med. Sci., **102**:25, 1891.
11. Vincent, E.: Considerations sur les caracteres anatomiques et sur le traitement des plaies par armes a feu de la moelle epiniere. Trois observations personelles de trepanation du rachis. Bull. et Mem. Soc. de Chir., **17**:674, 1891.
12. Prewitt, T. F.: Gunshot Injuries of the Spine with Report of a Case. Ann. Surg., **28**:187, 1898.
13. Alessandri, R.; and Mingazzini, G.: Beitrag zum Studium der durch Geschlosse erzeugten Ruckenmarksverletzungen. Monatschr. f. Psychiat., **24**:150, 1908.
14. Frazier, C. H.: Military Aspects of the Surgery of the Spine. Surg., Gyn. & Obst., **26**:589, 1918.
15. Craig, C. B.: Injuries to the Spinal Cord Produced by Modern Warfare. N. Y. Med. Jour., **104**:1035, 1916.
16. Hull, A. J.: Treatment of Gunshot Wounds of the Spine. Brit. Med. Jour., **1**:577, 1916.
17. Krause, F.: Die Kriegsverletzungen des Ruckenmarkes. Beitr. z. klin. Chir., **113**:222, 1918.
18. Symonds, C. J.: Laminectomy in Gunshot Injuries of the Spinal Cord. Lancet, **1**:93, 1917.

19. Holmes, G.: The Goulstonian Lectures on Gunshot Wounds of the Spinal Cord. Brit. Med. Jour., **2**:769, 815, 855, 1915.
20. Mauclaire, P.: Huit cas de plaies de la moelle. Bull. et Mem. Soc. de Chir., **40**:1128, 1914.
21. Ibid: A propos de l'extraction des projectiles intrarachidiens. Bu.l. et Mem. Soc. de Chir., **47**:1356, 1921.
22. Hassin, G. B.; Johnstone, K. L.; and Carr, A. M.: Bullet Lesion of Cauda Equina. J.A.M.A., **66**:1001, 1916.
23. Cumston, C. G.: The Treatment of Craniocerebral and Cord Injuries of Warfare. N. Y. Med. Jour., **109**:196, 1919.
24. Flourens: quoted by Wharton, H. R.: An Analysis of Three Hundred and Sixteen Cases in which Foreign Bodies Were Lodged in the Brain. Phila. Med. Times, **9**:493, 1878-9.
25. Regard, G. L.: Extraction d'Un Balle Situee dans le Ventricule Cerebral Lateral. Rev. Neurol., **26**:818, 1919.
26. Enderlen: Discussion at Deutsch. Gesellsch. f. Chir. at Brussels, April 7, 1915. Reported in Brit. Med. Jour., **2**: 190, 1915.
27. Vilvandre, G.; and Morgan, J. D.: Movements of Foreign Bodies in the Brain. Arch. Radiol. & Electrother., **21**: 22, 1916-17.
28. Weaver, J. C.: Wandering Bullet in the Brain. Intern. Clin., **1**:41st ser., p. 101, 1931.
29. Pilcher, C.: Penetrating Wounds of the Brain. Ann. Surg., **103**:173, 1936.
30. Mudd, H. L.: Discussion of paper of White, J. W.: The Surgery of the Spine. Trans. Amer. Surg. Assn., **9**:214, 1891.
31. Pyle, W. L.: Report of Two Cases of Laminectomy, with a Tabulated Collection of Fifty-Two Cases of Laminectomy of Recent Date. Ann. Surg., **19**:664, 1894.
32. Loison (no initials given): Coup de feu penetrant de la cavite sous-arachnoiddenne a la partie superieure de la region lombaire. Chute de la balle dans le cul-de-sac sous-arachnoiden ou on decouvre a la radiographie. Extraction. Bull. et Mem. Soc. de Chir, **27**:918, 1901.
33. Tuffier: Bull. Acad. de Med. (Paris), 63, 3rd ser., 452, 1910. Citrd by Mauclaire, ref. no. 21.
34. Auvray: Balle de schrapnell mobile a l'interieur du canal rachidien extraite au melieu des nerfs de la queue de cheval. Bull. Acad. de Med. (Paris), **76**: 3rd ser., 447, 1916.
35. Bulkley, K.: and Bergamini, H. M.: Removal of a Machine Gun Bullet from Sacral Canal. Surg., Gyn. & Obst., **29**:606, 1919.
36. Selberg, F.: Schrapnellkugel in der Cauda Equina. Wandern der Kugel in Duralsack. Zentralbl. f. Chir., **44**:162, 1917.
37. Roberts, C. W.: Gunshot Injuries of the Spine with Report of Two Cases. Sou. Med. Jour., **10**:734, 1917.
38. Potherat, E.: Projectile intrarachidien. Extraction. Bull. et Mem. Soc. de Chir, **39**:1233, 1913.
39. Fergor (no initials given): Balle intrarachidienne sans symptomes medullaires. Bull. et Mem. Soc. d'Anat. de Paris, **92**:166, 1922.

OSTEOCHONDRITIS DISSECANS AS RELATED TO TRAUMA*

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When osteochondritis dissecans is mentioned as a clinical entity, it is natural for one to visualize the classical picture, that of vague discomfort in the knee with increased disability after exercise and occasional swelling. With this there is x-ray evidence of a disturbed condition of the bone structure on the outer side of the inner condyle of the femur where an area of bone density is neatly surrounded by an area of bone rarity forming a pocket beneath the cartilaginous layer.

On the other hand, we may picture the process as having gone on to the stage where the pocket remains visible in the x-rays, but the dense central bone has wandered out into the joint cavity. The presence of the "joint mouse" frequently manifests itself by repeated lockage of the knee joint. The occurrence of this lockage may create a serious situation in this age of fast moving traffic.

Whereas the involvement of the outer side of the inner condyle of the femur is the most common site for the lesion, it may occur in many other localities and my reason for presenting this series of cases is to draw particular attention to two of unusual interest to me.

In one, there are the typical findings of osteochondritis dissecans in the carpal scaphoid and in the other the lesion was on the palmar surface of the semilunar.

Fig. 1
Oblique view x-ray showing osteochondritis dissecans in the spinal scaphoid.

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

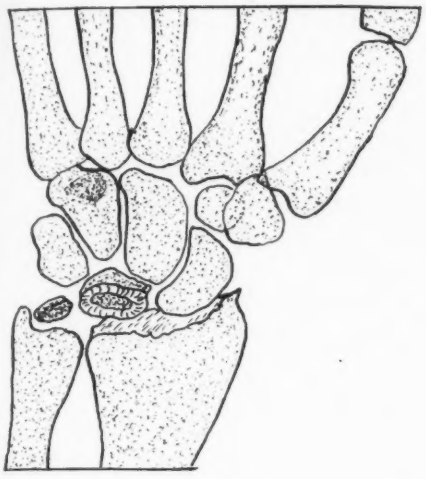

Fig. 2
X-ray tracing showing pocket in semilunar with osteocartilaginous body in ulnocarpal space.

The first case occurred in a 22-year-old white male. He gave a history of injury to his left wrist two years before examination. A year later the injury was repeated. However, the discomfort and loss of motion had been present for only five months. The x-ray (*Fig. 1*) showed an area of rarefaction in the thenar end of the scaphoid surrounding a bead like area of dense bone. This was removed at operation and found to be undergoing aseptic necrosis. Cultures were negative for any evidence of infection. Recovery was almost spontaneous, all swelling, pain and limitation of motion disappearing in about two weeks.

The second case was only recently seen. A 40-year-old white man had been employed for over twenty years in a cedar chest factory, where he handled 300 to 400 heavy chests daily, his work requiring him to put them under a "sander." Eighteen months before examination, one of the chests had slipped, twisting his wrist. He was temporarily disabled, but returned to his work. He again strained his wrist six months before examination. Since that time he has continued to work, but his efficiency has been greatly reduced due to the weakness and pain in his wrist. X-rays of the wrist showed the characteristic pocket in the palmar surface of the semilunar. The loose sphere of bone, however, had been expressed out of its former location by the edge of the radius when the wrist was in flexion. This fragment was found to be in the ulnocarpal space. Due to the repeated injuries both by the accident suffered and the wandering joint mouse, arthritic changes were shown to be present to a rather marked degree by the x-rays. Operation for the removal of this loose body has been recommended, but not yet carried out.

In addition to the above described cases there were, in my rather small series of twenty-three cases collected in the clinic of the University of Virginia Hospital, nine of the classical type involving the inner condyle of the femur. Two cases involved the outer condyle of the femur; three, the patella; one, the tibia anterior to the spines; one, the head of the femur (bilateral); one, the acetabulum (bilateral); two, the lumbar vertebrae; one, the tibia at the ankle; and one, the astragalus. Five of the cases had progressed to the stage where joint mice were present. Seventeen cases, or 74 per cent, gave a

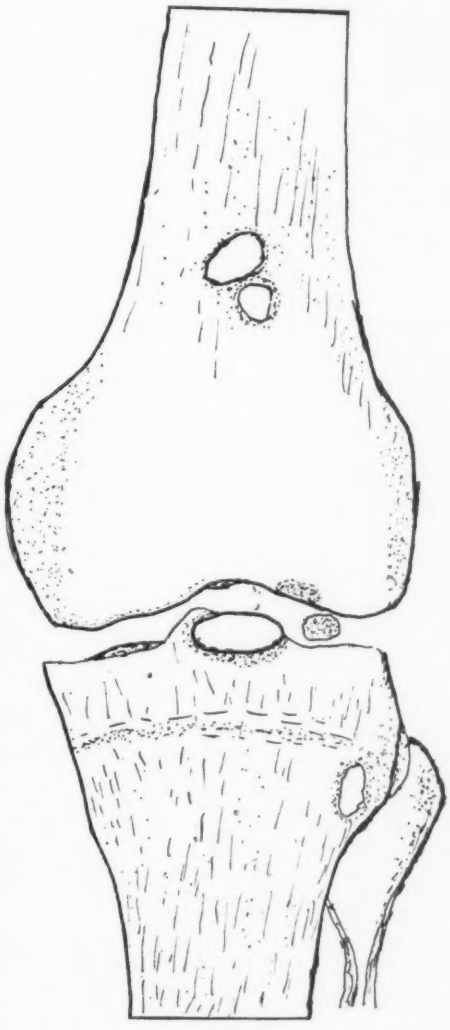

Fig. 3
Multiple loose bodies and irregularities in the surface of the femoral and tibial condyles from which they have arisen.

definite history of trauma. Of the remaining six cases one, a colored man with involvement of the inner condyle, was employed as a porter and worked a great deal on his knees.

Nine cases underwent operation and there was complete relief of symptoms in all but one. This was a 60-year-old man with multiple osteocartilaginous bodies and arthritic changes. His joint motion returned to normal, but he continues to have vague pains in his knee.

Fourteen cases were treated conservatively with casts or supports with recovery in seven, fair results in three, poor in one, and unknown in three.

The table at top of next page gives the statistics as related to age, sex, race and location of the lesion.

The traumatic factor was strikingly brought out in the case of a 14-year-old white boy who had a direct fall with his legs abducted. He was followed over a

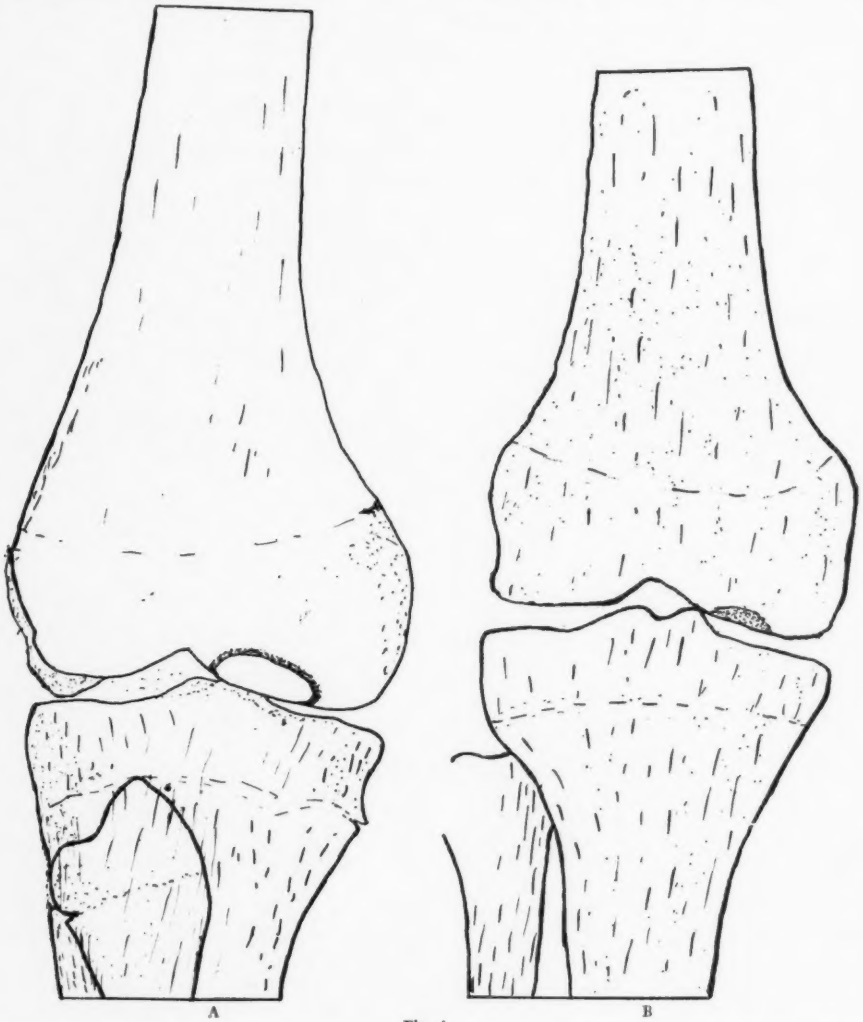

Fig. 4

(A) Oblique view showing typical large area of osteochondritis dissecans on the outer surface of the inner condyle of the femur and (B) a second view taken six months later showing the amount of filling in which has taken place.

ANALYSIS OF TWENTY-THREE CASES OF OSTEOCHONDRITIS DISSECANS

Age	Colored		White		Total
	Male	Female	Male	Female	
14			Acetabulum (bilateral) 1		1
15-20	F. condyle 1		F. condyle 2 Astragalus 1 Head femur (bilateral) 1	Patella (bilateral) 1	6
20-30	F. condyle 2		Vertebra 1 F. condyle 3 Tibia, lower end 1 Tibia, upper end 1 Patella 2		10
30-40			Carpal scaphoid 1	Condyle 1	2
40-50			Semilunar 1	Vertebra 1	2
50-70			Condyle (joint mice) 1	F. condyle 1	2
	3	0	16	4	23

period of two years and during the second year complained of intermittent pain in both hips. When the first x-rays were taken, they showed what appeared to be a detached fragment at the upper margin of each acetabulum. In the course of ten months, as shown by x-ray, these fragments had become contiguous with the rest of the acetabular lip. However, five and a half years later, they reappeared as typical areas of osteochondritis dissecans. Unfortunately the case was not followed further in spite of our repeated efforts to get in contact with him.

A peculiar condition was found at operation on a 28-year-old colored man who, four days previous to first examination, gave symptoms and signs typical of a ruptured semilunar cartilage, although he complained of periodic attacks of pain in his left knee since a severe injury eight years before.

The cartilage was found to be split through its center and of the bucket-handle type. When the posterior end of the handle portion of the cartilage was removed, there was attached to it an osteocartilaginous body which by traction became evulsed from its bed in the tibia. This man recovered and was symptom-free when seen twenty-seven days after operation.

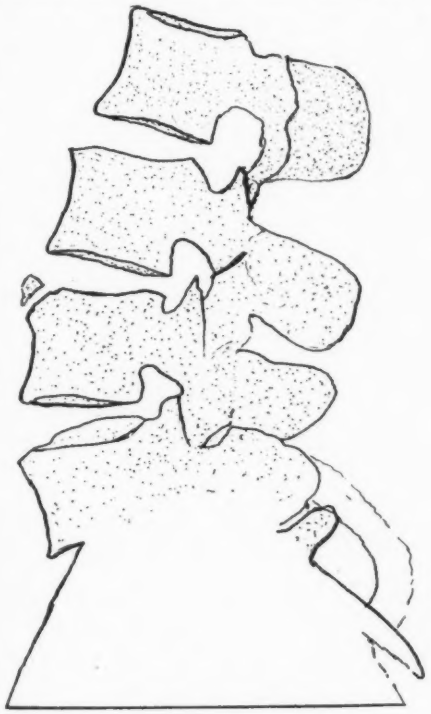

Fig. 5
Osteochondritis dissecans of the fourth lumbar vertebra.

Fig. 6
Osteochondritis dissecans of both femoral heads.

Trauma has been generally accepted as the most logical cause of osteochondritis dissecans. One or two other theories have been advanced. Heredity was suggested by Bernstein, Wagner and Cohn, and Weil because of the similarity of cases they found in members of the same family. Archer and Peterson drew attention to its similarity in cases of hip involvement to Perthes'.

From a survey of over forty articles and case reports, one finds that the authors usually attribute the cause to trauma either as one severe injury or repeated injuries of a lesser degree. They agree in general that a localized reaction occurring in any of the various joints involved is one of a localized area of aseptic necrosis simulating an infarction.

Since the cartilage derives its nutrition from the synovial fluid, it retains its continuity for a long period of time before the necrotic bone is allowed to work its way out into the joint cavity. When it does, however, the same nutritional properties of the synovial fluid may be an important factor in supplying a cartilaginous covering and in some instances actually increasing its size.

It has been my experience that in most of the cases the deficiency created by the expulsion of the necrotic bone gradually disappears. This seems to be enhanced to some extent by a gentle curetting of the base of the cavity.

SUMMARY AND CONCLUSIONS

In a survey of the literature there is found to be a fairly constant history of trauma related to the development of osteochondritis dissecans. In this small series of twenty-three cases, seventeen gave a definite history of trauma to the involved joints while one of the remaining six spent many hours daily working on his knees. One case was associated with rupture of the internal semilunar cartilage and, following the removal of the cartilage and osteocartilaginous body, there was entire freedom from symptoms in four weeks.

The classical case of osteochondritis dissecans shows on x-ray examination involvement of the inner condyle of the femur.

The lesion was bilateral in three of the reported cases, namely: in the patella, head of the femur and acetabulum.

A case with osteochondritis dissecans of the carpal scaphoid and another of the semilunar are herewith reported. As far as can be ascertained from a review of the literature, these are the first lesions to be reported in these bones.

REFERENCES

1. Fairbank: Brit. Jour. Surg., **21**:67, July, 1933.
2. Frieburg: Jour. Bone & Joint Surg., **57**:3, Jan., 1923.
3. Phemister: Jour. Bone & Joint Surg., **58**:278, April, 1924.
4. Archer and Peterson: Sou. Med. Jour., **23**:611, 1930.
5. Balensweig: Osteochondritis of the Knee. Jour. Bone & Joint Surg., **7**:465, 1925.
6. Buchman: A Resume of the Osteochondritides. Surg., Gyn. & Obst., **49**:447, 1929.
7. Kohler: Roentgenology, p. 211. New York: Wm. Wood & Co., 1929.
8. Brackett: Jour. Orthop. Surg., **15**:79, Feb., 1917.
9. Lange: Zeits. f. orthop. Chir., —:268, March, 1929.

REPAIR OF OLD MUSCLE TENDON AVULSIONS*

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Spontaneous ruptures either of muscles or of tendons is an infrequent injury as compared to traumatic severance of either one, and in my experience the avulsion of a tendon from its attachment to its muscle is a still more rare injury. The available literature is also lacking in case reports.

I wish to report herewith a spontaneous rupture of the long head of the right biceps branchii muscle from its attachment to the muscle belly, together with its successful repair by a method original with me, and so far as I can find in the available literature, not heretofore described.

H. H., aged 40, white, an automobile mechanic, had had measles, whooping cough, mumps, malaria in 1904; gastric ulcers three years previously; nasal septum operation in 1920. His father and mother were living and well; one brother was living and well; three brothers had died of pertussis, pneumonia and tuberculosis, respectively. Laboratory examinations showed a urine of 1.025, acid, and negative; white blood cells 7,800, sugar 95 mg., nonprotein nitrogen 33, Kahn and Wassermann tests negative, blood Type II. He was lifting a heavy auto truck radiator on August 7, 1934, when his partner released it too soon, leaving its full weight on the patient to support. He felt something tear in

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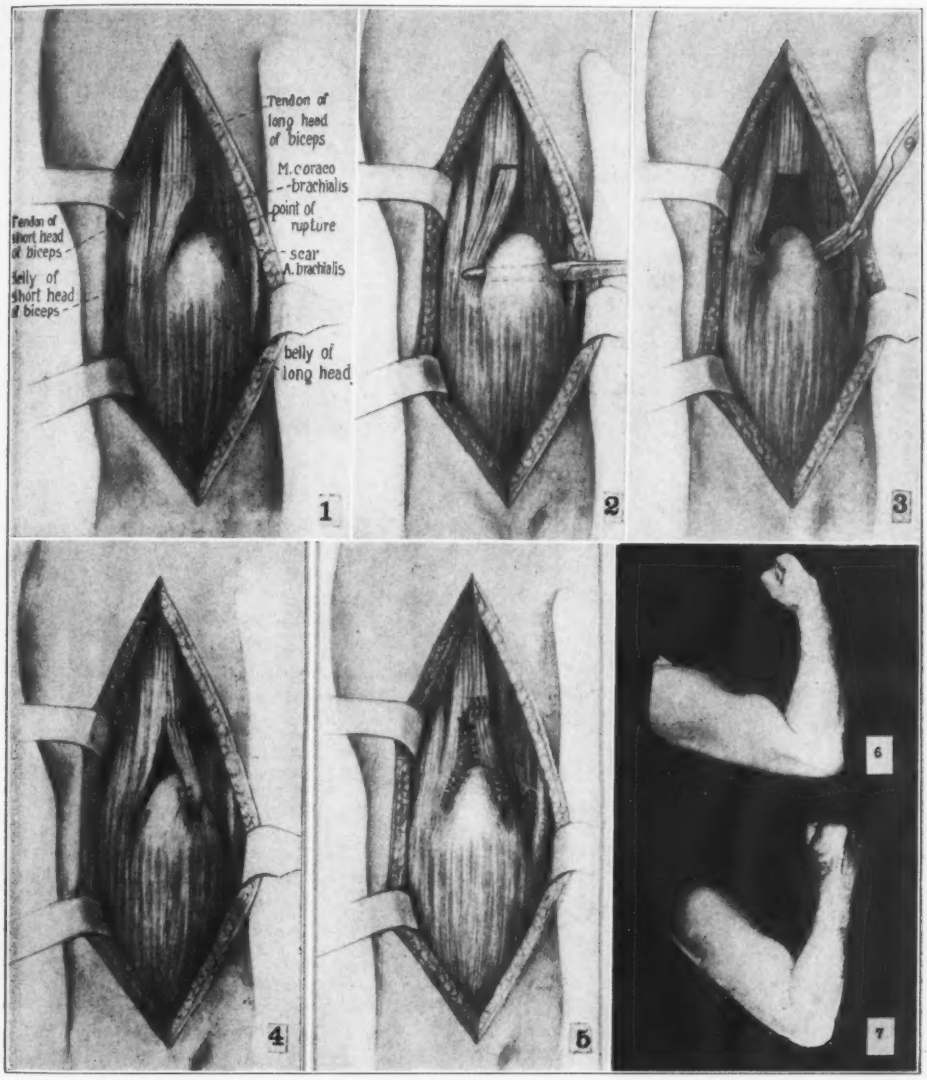

Fig. 1. Ruptured long head of biceps muscle. Fig. 2. Tendinous head split and tunnel formed through conical end of muscle belly. Fig. 3. Split tendon drawn through tunnel. Fig. 4. Same as Figure 3. Partially sutured. Fig. 5. Same as Figure 3. Completely sutured. Fig. 6. Arm before operation. Fig. 7. Arm after operation with biceps contracted.

his right arm, but as it was near quitting time he did not seek medical advice until the next morning, when his arm was sore and had little lifting power. His family physician treated it conservatively.

About seven weeks later, the regular insurance physician, Dr. G. R. Northrup, was put in charge of the case, which was thought to be a muscle hernia. He was accordingly operated upon at St. Mary's Hospital on October 9, 1934. The operative findings were hernia in the fascia of the biceps, with relaxation of the belly of the muscle. Hernia in the fascia was repaired and relaxed long head, suturing the belly of the muscle to the tendinous long head. His arm was kept in a sling most of the time. The wound healed kindly, but disability returned. Evidently the muscle belly did not unite to its tendinous head.

On December 20, 1934, the insurance company's surgeon and an official referred him to me, and the following subjective and objective findings were noted: on attempts to contract his right biceps or supinate the forearm two distinct muscle bellies could be observed, one nearly normal in position and the other nearer the elbow (*Fig. 6*). He likewise complained of severe throbbing pain in his operation scar, together with some numbness, but not complete loss of sensation in the palm of his hand. His hand became numb upon flexing the arm, but felt colder than the other. The radial pulse was fairly good. He also complained of inability to abduct the arm more than about 30 degrees. There was atrophy of his right deltoid with pains in that shoulder. There was also about 50 per cent limitation of motion in the right wrist. These two latter conditions were probably due to disuse.

I diagnosed the condition as a ruptured biceps muscle, with disuse atrophy of the right deltoid muscle, scar tissue contraction of the right pectoralis major muscle, and disuse stiffness of the right wrist. I advised operative repair.

On December 31, 1934, at St. Mary's Hospital, under ethylene anesthesia, I excised the scar of the previous operation on the antero-medial aspect of the right arm. I then isolated the biceps muscle and its heads, noting that the short head of the biceps was intact and normally blending with its muscle belly. The tendinous long head had been avulsed from its segment of the muscle belly (about two-thirds of this particular muscle, it seemed to me) and was slightly adherent to its posterior surface, probably the septum between the two muscle portions. The lower end of the tendinous head was a firm, whitish bundle, almost transverse and about 2 cm. broad. The upper end of the muscle body was conical and consisted of old tough scar firmly binding the connective tissue sheaths of the muscle fibers and septa and reuniting them strongly at the upper end (*Fig. 1*). When he attempted to contract the right biceps that portion originating as the short head contracted, forming the usual prominence but of lesser degree, while the portion avulsed from the long head contracted and formed a prominence near the elbow. This condition was not quite anticipated before operation, as I thought the injury probably was a tear of the entire biceps through its middle.

The problem was one of uniting the tendinous long head with the now conical scar where it was avulsed from its belly. Obviously the union should be strong enough to do heavy work, and also to permit normal muscle contraction without friction against surrounding structures, as would result if an uneven or irregular anastomosis with nodules or lumps were made. I thought of end-to-end suture, but felt it would be apt to pull apart again under violent strain. Suturing the tendinous head on one surface of the belly (as seemed to have been done before), if it healed, would not result in an even pull on all fibers, and this plan was discarded. I then decided to form a sling or stirrup from the long head by cutting across half its fibers about 4 cm. from the lower end (*Fig. 2*), then splitting it to within 1 cm. of the lower end, which had already healed into a tough scar. I made a transverse tunnel (similar to that used when anchoring a narrow tendon to bone) through the upper end of the muscle belly (*Figs. 3* and *4*), drew the tendinous flap through this tunnel back to its point of severance and sutured it there with silk. I next sutured the sides of this tendinous loop to the conical scar (*Fig. 5*) and sutured all to the short head of the muscle for further support. This was so planned in length as to draw the muscle belly into normal tension and position. This gave a strong, even attachment by passing under the old conical scars, as well as being united along the sides. It had a fairly smooth, tapering anastomosis.

If the tendinous fibers had not been firmly bound together at their lower end, I would have split the tendon upward and made two oblique tunnels with a common opening at the apex of the conical scarred end of the muscle belly and extending outward to the muscle sides, drawing a split tendon end through each tunnel and suturing it at the side openings as well as at the center or tunnel entrance. If too much slack were present, I could bring the tendon ends back along the conical end to the tunnel entrance and suture them to the tendon as well as to the cone sides. However, I could have split the tendon upward, drawn one end through the tunnel, sutured it to its mate, and slipped the loop back into the tunnel with the tendon suture line in the middle of the tract, then completing the operation as in plan number one. As before stated, I chose the first method described as it gave me the proper length, and its lower end seemed quite strong.

Manipulation of the forearm now showed a normally acting biceps muscle. However, the arm could not be abducted from the body more than about 40 degrees even under anesthesia, due to a disuse contraction of the connective tissue of the pectoralis major muscle and the costocoracoid membrane. It was necessary to lengthen its tendon of insertion by cutting it quite obliquely and resuturing to permit of 90 degrees abduction with the forearm at right angles. After two weeks, passive and active motion and diathermy were given. He left the hospital on January 19 with the wound completely healed. His only complication had been a mild laryngitis on January 14. The throbbing pain and numbness had disappeared on awakening from the anesthetic. The return of the biceps function was practically complete after two months. However, the deltoid atrophy was slow in improving, as was the stiffness in his right wrist. He was able to resume his work, with heavy lifting alone prohibited, after thirteen weeks (*Fig. 7*).

I doubt that the above described methods would be as satisfactory for immediate suture of such fresh injuries, but where the muscle end is firmly held by old scar, it proved an ideal means of restoring function. The method so far as I know has not been previously described.

HYPERPLASIA OF ENDOMETRIUM: A STUDY OF ENDOMETRIUM AFTER TREATMENT*

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The term "hyperplasia of the endometrium" was employed first in 1913 by Cullen at the suggestion of Dr. William H. Welch (Novak 1917).[65 60] Various other descriptive terms previously had been applied: chronic hyperplastic endometritis, endometritis fungosa (Olshausen 1875);[75] endometritis ovarialis (Brennecke 1882);[8] metrorrhagia myopathica (Anspach); insufficientia uteri (Theilhaber); polypoid endometritis; dysfunctional bleeding; endometritis postmenstruationem incompletam (Driessen 1914).[22] The epochal studies of Hitschmann and Adler (1908)[41] had paved the way for its clear differentiation from the phases of normal menstruation. The fruitful endocrine studies of the past decade have led to a better understanding of the etiologic factors. Certain ones of the recently isolated sex hormones have been employed in treatment, results of which have not been uniform. We shall present our clinical experience with some of these active principles, paying especial attention to the endometrium following therapy.

PATHOLOGY

A brief summary of important recent studies of the pathology and hormonology is indicated. Cullen (1913)[20] described the appearance of the hyperplastic endometrium, emphasizing the necessity of its differentiation from adenocarcinoma. Schröder (1915),[85] apparently unaware of Cullen's work, used the term "hyperplasia of the endometrium" in a description of the characteristic ovarian and endometrial changes which he thought were primary in the ovaries. In 31 cases both the ovaries and the endometria were studied and in only two cases were corpora lutea found, one of which was degenerated, and the other, a very recent one, was thought to have been of traumatic origin. Characteristic ovarian findings included numerous follicular cysts which were lined by well preserved granulosa cells, often showing mitotic figures. These cysts, frequently containing apparently undegenerated ova, were accompanied often by marked theca interna proliferation. Schröder believed that stimulation by the persistent follicle, which had failed to rupture and to form a corpus luteum, accounted for the endometrial hyperplasia. The infrequent occurrence of corpora lutea in the ovaries in this condition has been verified by Babes (1924),[4] Novak and Martzloff (1924),[67] Shaw (1929)[88] and Fluhmann (1931).[24 26] Burch and his coworkers (1934)[12] believe that their occasional presence can be attributed either to "diagnostic errors, non-functioning corpora or spontaneous and induced ovulation." Hofbauer (1930, 1931)[42 43] first produced hyperplasia experimentally by the injection of guinea pigs with fresh extracts of anterior lobe of pituitary. Burch and his coworkers (1931,1932)[9 10 11 50 101] apparently have confirmed Schröder's concepts as to etiology by producing similar endometrial changes from injections in spayed rodents of follicular fluid from the ovaries in hyperplasia and from injections of estrogenic extracts and of solutions of crystalline theelin. Additional evidence was adduced by the production of a hyperplastic type of endometrium in the human castrate following injections of theelin (Werner and Collier, 1933).[97] Similar effects were obtained following injections of a benzoic acid ester of dihydro-estrin (Kaufmann, 1933).[46]

FUNCTIONAL LEVEL OF OVARY AND ANTERIOR PITUITARY AND THEIR INTERRELATION

Schröder's concept as to the ovario-endometrial pathology is accepted generally; however, there is no uniformity in opinion as to the actual level of ovarian function, or as to the role of the pituitary or even as to the primary factors in the actual production of bleeding. Opposed to Schröder's views Shaw (1929)[88] believes that the endometrial involvement is primary and that thereby the function of the ovaries is inhibited with the result that an ovarian toxin is formed which acts upon the endomertium, producing bleeding. Studies of blood and urinary estrin values as described by Frank (1929)[28] have not yielded uniform results in the hands of Mazer and Hoffman (1929),[55] Siebke (1929),[91] Zondek (1930),[102 103] Frank (1931),[29] Mazer and Goldstein (1932),[56] and Kurzrok and his coworkers (1932).[54] Reports by Fluhmann (1931)[24 25 26] and Mazer and Goldstein

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(1932)[56] indicate an increased blood level of anterior lobe pituitary fractions. Smith and Rock (1933)[93] found follicular ripening principles in the urine of 14 out of 18 patients with menometrorrhagia. Burch (1934)[12] has found no records of histological studies of the human pituitary gland from patients exhibiting endometrial hyperplasia.

Burch and his coworkers (1931)[9 10] consider that there is "a disturbance of the hypophyseal-ovarian relationship." Novak (1932)[69] believes that the balance between the ovarian stimulating hormones of the anterior lobe is upset. Burch and his coworkers (1934)[12] are of the opinion that ovarian hyperfunction probably occurs in the younger group of patients with the result that the function of the anterior lobe is depressed by the excess estrin so that adequate ovulational stimulation does not occur. They believe the ovaries in the older group of patients to be refractive to pituitary stimulation, even though functioning at a higher level than normal, so that ovulation and corpus luteum proliferation does not occur. We are inclined to agree with Burch's ideas regarding possible differences in the ovario-hypophyseal relationship in the two age groups. We have been impressed with differences in the clinical symptoms and findings in these two groups. Often in the younger patients the amenorrhea (primary polyhormonal amenorrhea of Zondek, 1934)[104] is as striking as the hemorrhage, whereas in the older group menorrhagia of fairly cyclic character is common. The former group is often hyper-feminized, while many of the latter group show regressive primary and secondary sexual menopausal changes. The former exhibit enlarged cystic ovaries, while as a rule the ovaries in the latter group may be normal size or even sclerotic. These variations are believed to explain, in part, the apparent differences in the ovarian responses of the two groups of patients to extracts of APL/PU* (Hamblen, 1933,[37] 1935,[38] Hamblen and Ross, 1936):[39] inability to induce ovulation and corpus luteum proliferation in the younger patients, while, on the other hand, recent corpora lutea were found quite uniformly in the older age group. It was felt that, perhaps, the younger ovary being quite sensitive to the follicle-stimulating principle of extracts of PU, responded by even further cystic degeneration and increase in the hyperestrinism. Cessation of bleeding when it occurs in these cases after such injections may be due to increased estrin formation allowing more adequate endometrial circulation or nutrition. It was suggested that the ovaries in the older age group responded to PU extract injections by ovulation, since there were few follicles to be stimulated and little estrin thereby to be formed which might depress anterior lobe function.

*APL/PU used throughout to indicate the so-called anterior pituitary luteinizing principle of pregnancy urine; PU refers to pregnancy urine; APH refers to true extract of anterior lobe pituitary containing gonadotropic principle.

MECHANISM OF BLEEDING

There are widely divergent opinions regarding the mechanism of bleeding. Graves (1930)[34] emphasized the failure of desquamation of the endometrium and the constant clotting of the resulting blood. Burch (1934)[12] has been impressed with the possible role of traumatism as suggested by Seitz (1922)[87] and has observed hemorrhage in adjacent superimposed portions of endometrium. We believe with Burch and Burch (1933)[14] that decrease in the level of estrin below the amount necessary to maintain adequate endometrial growth and circulation is an important factor in the initiation of bleeding. Necrosis of sites of impaired circulation may be the actual cause. Such isolated areas of necrosis are observed commonly. Mikulicz-Radecki (1929),[62] upon studying the bleeding endometrium *in situ* with his hysteroscope, found frequent changes, localized hemorrhages from vessels and from local endometrial lesions. Novak (1932),[69] emphasizing the frequently observed intactness of the endometrium, suggested bleeding might be due to increased permeability of the endometrial vessels.

AGE INCIDENCE AND ASSOCIATION WITH OTHER PELVIC DISEASES

Hyperplasia of the endometrium is observed more commonly at or near menopause. Schröder (1924)[86] found 8 to 9 per cent of patients were between 16 and 20 years of age; and 8 to 9 per cent between 20 and 37 years of age; and from 82 to 84 per cent were 37 years and older. The post-menopausal endometrium may be very thin and atrophic with dilated interval glands. The endometria and ovaries of fetuses or of the new born may show changes similar to those observed in endometrial hyperplasia of the adult. The cause of the changes is not known, but Spivak (1934)[94] suggests that they may be due to action of the fetal hypophysis.

King (1933)[48] believes that hyperplasia of the endometrium may be responsible for bleeding in many patients with fibromyomata. He found that 71 per cent of fibromyomata treated with

radium show hyperplasia. Witherspoon (1933)[99] believes that the etiology of endometrial hyperplasia and of fibromyomata may be similar. Witherspoon and Butler (1934)[100] suggest that inflammatory changes in and about the ovaries may result in endometrial hyperplasia. Localized hyperplasia may be observed in association with endometrial polypi (Novak, 1933).[70 71] Novak also notes that it may be observed in connection with endometrial implants. Cullen (1928),[21] Hintze (1929),[40] Taylor (1932),[96] and Novak (1933)[70 71] could find no etiologic connection between endometrial hyperplasia and adenocarcinoma. The endometrium in patients exhibiting granulosa cell carcinomata of the ovaries often shows hyperplasia (Novak, 1933).[70 71]

DIAGNOSIS

Burch (1934)[12] emphasizes the diagnosis may be warranted because of "a thick stroma, an exceptionally large number of glands, or an abnormal multiplication of cells," and he uses the term to apply to patients "exhibiting an abnormal increase in the elements of the endometrium, an absence of functioning corpora lutea and a profuse and irregular hemorrhage." Burch includes as hyperplastic those cases in which there is bleeding from an essentially normal interval endometrium, but he suggests that "aluteal bleeding" would be a better general term. We believe that the amenorrheic phase, as well as the hemorrhagic one, should be stressed in any system of classification. Many pathologists and clinicians prefer not to make a diagnosis of endometrial hyperplasia without the presence of the swiss-cheese pattern, as emphasized in various articles by Novak and others.[63 84] It may be that future studies will lead to a satisfactory grouping of functional disorders of menstruation based on etiology, histopathology, and symptoms. While we agree in general with Burch's criteria of diagnosis and favor the general term "aluteal bleeding," in this report we present only cases which showed "glandular hyperplasia" of the swiss-cheese type.

TREATMENT

Some of the recent reports of attempted conservative therapy of hyperplasia of the endometrium in the younger group of patients are reviewed. The theoretical mode of action of a number of therapeutic agents is presented graphically in *Fig. 1.* Since radiotherapy is effective and not contraindicated when necessary in treating patients nearing menopause, therapeutic consideration of the older age group patients is omitted.

Thyroid Extract.—Despite the new ovarian and pituitary hormones, many clinicians reaffirm their faith in thyroid medication. Plass (1931)[79] advises its use in all adolescent patients with excessive menses whether basal metabolic rate be low or normal. Cooke (1931, 1932)[17 18] and Anspach and Hoffmann (1933)[2] consider it valuable, the latter having found little service in PU extracts. Kretzschmar (1933)[53] finds thyroid therapy effective in 73.9 per cent of his patients. King (1933),[48] Bram (1934)[7] and Mussey and Haines (1934)[64] note close association of thyroid dysfunction and menstrual disturbances and deem thyroid therapy rational and effective.

Estrin is of no value (Mazer and Ziserman, 1932)[57] and even productive of harm (Mazer and Goldstein, 1933);[58] Pratt (1932)[80] found it of no service. Hamblen (1931, 1933)[35 37] has observed occasionally cessation of excessive bleeding following its exhibition, and attributes this temporary effect to increasing the estrin level, allowing more effective endometrial circulation. Burch (1935)[13] has observed similar cases. Novak (1935)[73] observes that this type of therapy is not logical, but that actual bleeding may be warded off.

So-called Anterior Pituitary Luteinizing Principle of Pregnancy Urine (APL/PU).—Zondek (1930)[102 103] and Campbell and Collip (1930)[16] first reported clinical employment of this principle, the latter using Collip's placental extract. Novak and Hurd (1931)[68] and Smith and Smith (1931)[92] reported excellent and prompt control of excessive bleeding following its use, the former in 44 out of 51 patients, the latter in 19 patients. Geist (1935),[33] in discussing Novak's report before the American Gynecological Society in 1931, reported 24 patients similarly treated in whom no striking therapeutic effect was obtained. Hamblen (1932),[36] Johnstone, Wiesner and Marshall (1932),[44] J. Novak (1932)[74] and Anspach and Hoffmann (1933)[2] found it of apparent value in a small number of instances. Klingler and Burch (1933)[51] and Burch and Burch (1933)[14] note that excessive bleeding may be stopped without progestational proliferation of the endometrium. Smith and Rock (1933)[93] found only two patients out of 56 who failed to be benefited promptly; 50 per cent of those treated had subsequent regular and normal menses; the patients varied in ages from 14 to 47 years. Rock (1933)[81] observed that while APL/PU will relieve certain cases, it will not benefit all and will permanently cure only a

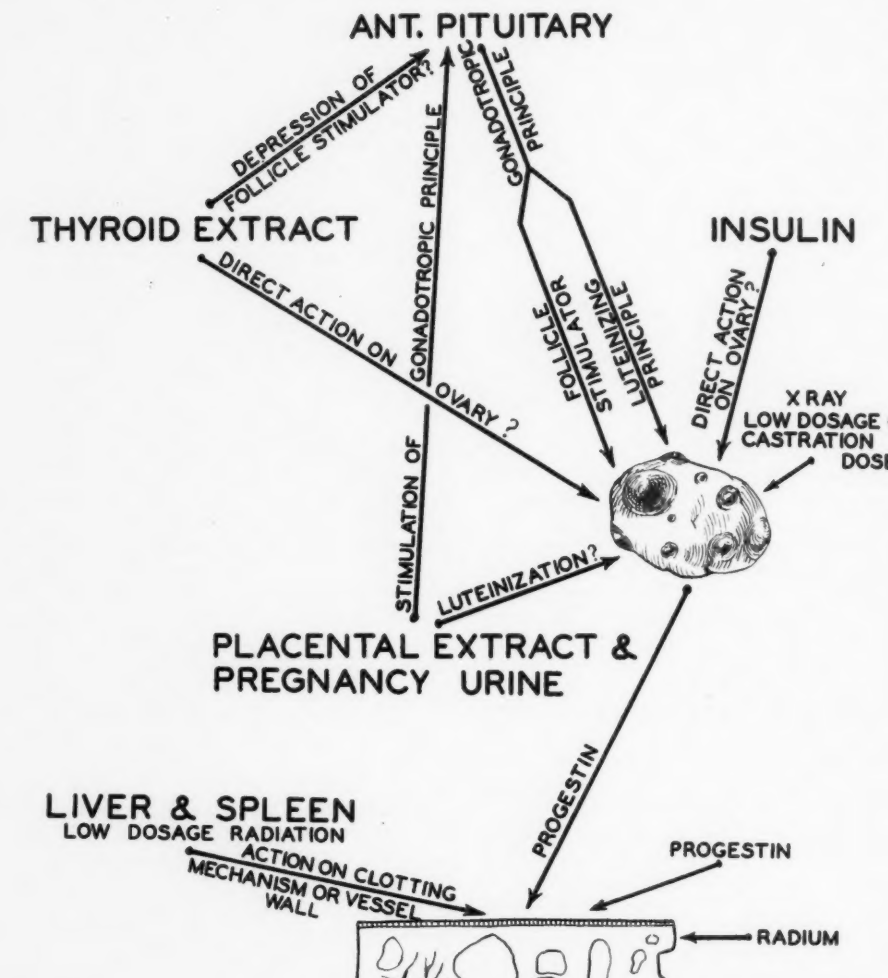


Fig. 1

Diagram of the theoretical methods of action of some of the therapeutic agents used in endometrial hyperplasia.

few. Novak (1933)[70 71] reported good results from the treatment of over 200 patients. Mazer and Goldstein (1933)[58] recommended low dosage radiation of the ovaries and pituitary in patients refractive to APL/PU extracts and Mazer and Katz (1934)[59] observe that 80 per cent of women under 40 years of age respond at least temporarily to APL/PU, the results being better if placental extract is employed also. Gabrielianz (1934)[32] obtained good results from placental extract alone. Frank, Goldberger and Spielman (1934)[31] and Geist and Spielman (1935)[33] find APL/PU ineffective and place chief reliance on moccasin venom therapy. We (Hamblen, 1933, 1935, Hamblen and Ross, 1936)[37 38 39] have been unable to affect favorably excessive flow in the majority of young patients by APL/PU injections; our chief reliance at present is on treatment with snake venom.

Progestin has been available for clinical trial only in limited quantities and for a short period of time; however, encouraging reports of its employment have appeared. Kaufmann and Bickel (1932),[45] Knab (1933),[52] and J. Novak (1932)[74] have found it of value. Mazer and Katz (1934)[59] observe that, while it is rational therapy, its effect is temporary and only substitutive. Corner (1935)[19] says:

> "Here, then, is a definite hormone about to be handed to the medical profession to take the place of the meaningless corpus luteum preparations of the past. It has the property of bringing about premenstrual changes and the uterine condition of early pregnancy. What is to be done with it? * * * Progestin might be useful * * * in menorrhagia when (if ever) it is due to overaction of estrogenic substance."

Snake venom therapy first was described by Peck (1932).[76] Subsequent reports have indicated its beneficial effect in controlling excessive uterine bleeding. (Peck and Goldberger, 1933;[77] Frank, Goldberger and Spielman, 1934;[31] Geist and Spielman, 1935;[33] Peck and Rosenthal, 1935).[78] Its beneficial action is said to be exerted on the vessel walls and on the clotting mechanism.

Other methods include stimulative low-dosage radiation of ovaries and pituitary and, in some instances of liver and spleen (Stephan, 1920;[95] Ford and Drips, 1929;[27] Werner, 1931;[98] Burnam, 1933;[15] Mazer and Goldstein, 1933).[58] There are many who use small dosage of radium (Keene and Payne, 1933)[47] and in cases refractive to other measures radiotherapy or hysterectomy will offer the only method of cure. Elden (1934)[23] has reported good results from oral administration of enteric coated desiccated anterior lobe extract in massive doses up to 75 grains. Klaften (1935)[49] found some cases benefited by insulin therapy. Parathyroid extract and calcium preparations have been found to be of value (Allen and Goldthorpe, 1929);[1] Bakacs, 1933).[3] Rossak (1933)[83] reported good results following intravenous injections of 1 per cent aqueous Congo Red. At present one of us (Hamblen) is studying the clinical, ovarian and endometrial responses following injections of an active gonadotropic extract of anterior lobe of pituitary (APH).

It would seem from these reports that no one principle (with the exception of radiotherapy and hysterectomy) as employed at present can be relied upon to cure all cases of adolescent menometrorrhagia. In part, the variance in the results of therapy may be attributable to the different methods employed in evaluating treatment. Cessation of a prolonged spell of bleeding following therapy, even if subsequent menses prove regular in rhythm and flow, cannot be taken as incontestable evidence of cure. Spontaneous remissions occur; long periods of amenorrhea may intervene; anovulatory bleeding, strongly urged by Novak (1934)[72] and supported by Bartelmez (1933)[6] and bitterly opposed by Shaw (1934, a and b),[89 90] may be confused with normal secretory menstruation. More critical appreciation of the effectiveness of hormonal treatment may be sought in the study of ovaries, of endometria and of hormonal urinary and blood levels following therapy. Hamblen (1933, 1935, and with Ross, 1936)[37 38 39] was unable to find evidence of induced ovulation or corpora lutea formation in the ovaries of younger patients (ages 16 to 34) following APL/PU injections, but observed uniformly recent corpora lutea in the ovaries of the older patients. Endometrial biopsies, taken by the suction (Klingler and Burch)[50] or the punch (Burch, 1935)[60] method allow the endometrial changes to be followed. Errors in the interpretation of results obtained from biopsies are quite likely to occur, for Bartelmez (1931)[5] has shown that "variability in different regions of the same mucous membrane is a constant feature during menstruation as well as at other stages of the cycle." Klingler and Burch (1933),[51] McClellan, Phelps and Burch (1935),[60] and Rock (1935)[82] have studied by this method endometria following APL/PU therapy, and have failed to observe any progestational proliferation despite apparent clinical benefit. Blood and urinary studies of hormonal concentrations in untreated cases

have yielded no uniform results which might be utilized in following the course of therapy.

DATA AND RESULTS

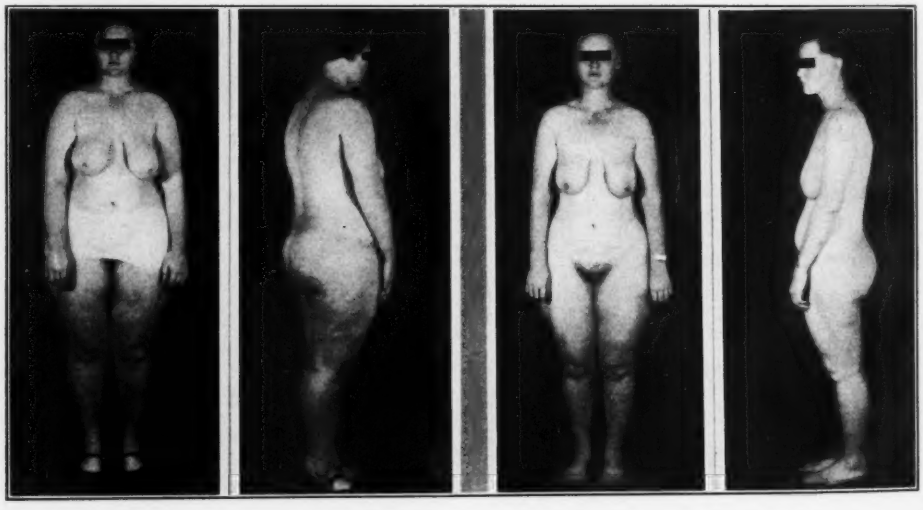
We have followed 27 patients in the younger age group with frequent endometrial biopsies during various types of therapy. These patients were selected because of severity of their symptoms and because they had proven refractive to many of the usual conservative methods of treatment. Since in many instances curettage had been done or had become necessary as a temporary therapeutic measure, biopsies were not begun or therapy evaluated until the resumption of excessive bleeding after the curettage. Biopsies were taken at frequent intervals both in the bleeding and in the non-bleeding stages. Each time at least two biopsy specimens were taken from different portions of the endometrium to reduce the error inherent in this method of obtaining tissue. The period of these studies has extended for two years in one case and in no instance has it been for less than two months. As we have observed previously, all these patients showed a typical "swiss-cheese" endometrial pattern. The ages varied from 14 to 34 years. The distribution of patients as to the type of therapy employed is:

APL/PU ("antuitrin S"), 10 patients;
APH (gonadotropic principle from extracts of anterior lobe of pituitary ("antuitrin, gonadotropic"), 6 patients;
Moccasin venom, 7 patients;
Thyroid extract, 2 patients;
Progestin ("proluton"), 2 patients.

In addition two of the above patients received low-dosage x-ray radiation of the ovaries and pituitary without avail while under observation.

Dosage.—APL/PU was given subcutaneously in doses of 200 to 400 rat units three to four times daily for from four to ten days. Gonadotropic extract of anterior lobe was employed in doses of 20 to 30 R. U. twice or three times daily for four to eight days. Moccasin venom (1:3,000 dilution) was used in 0.2 to 0.4 c. c. doses twice weekly for from two to four months. Thyroid extract was given as tolerated. Progestin ("proluton") was given in one instance in 2/5 European rabbit unit doses once to three times daily for three days on two occasions; and in another instance in 1 European rabbit unit dose daily for five days. Larger dosage of progestin could not be employed or more patients treated because of the small amount of the principle available to us. Further studies with progestin are under way at present.

As judged by an arbitrary clinical standard of cessation or decrease in excessive uterine bleeding within five days from the time of the first injection and/or of warding off further ex-



A B

Fig. 2

Photographs showing weight loss following reduction diet and thyroid therapy.
(A) Patient, G. H., 1/4, '34. Weight 205 pounds, B.M.R. plus 7 per cent (B) Patient, G. H., 6/28, '34. Weight 168 pounds, B.M.R. minus 4 per cent.

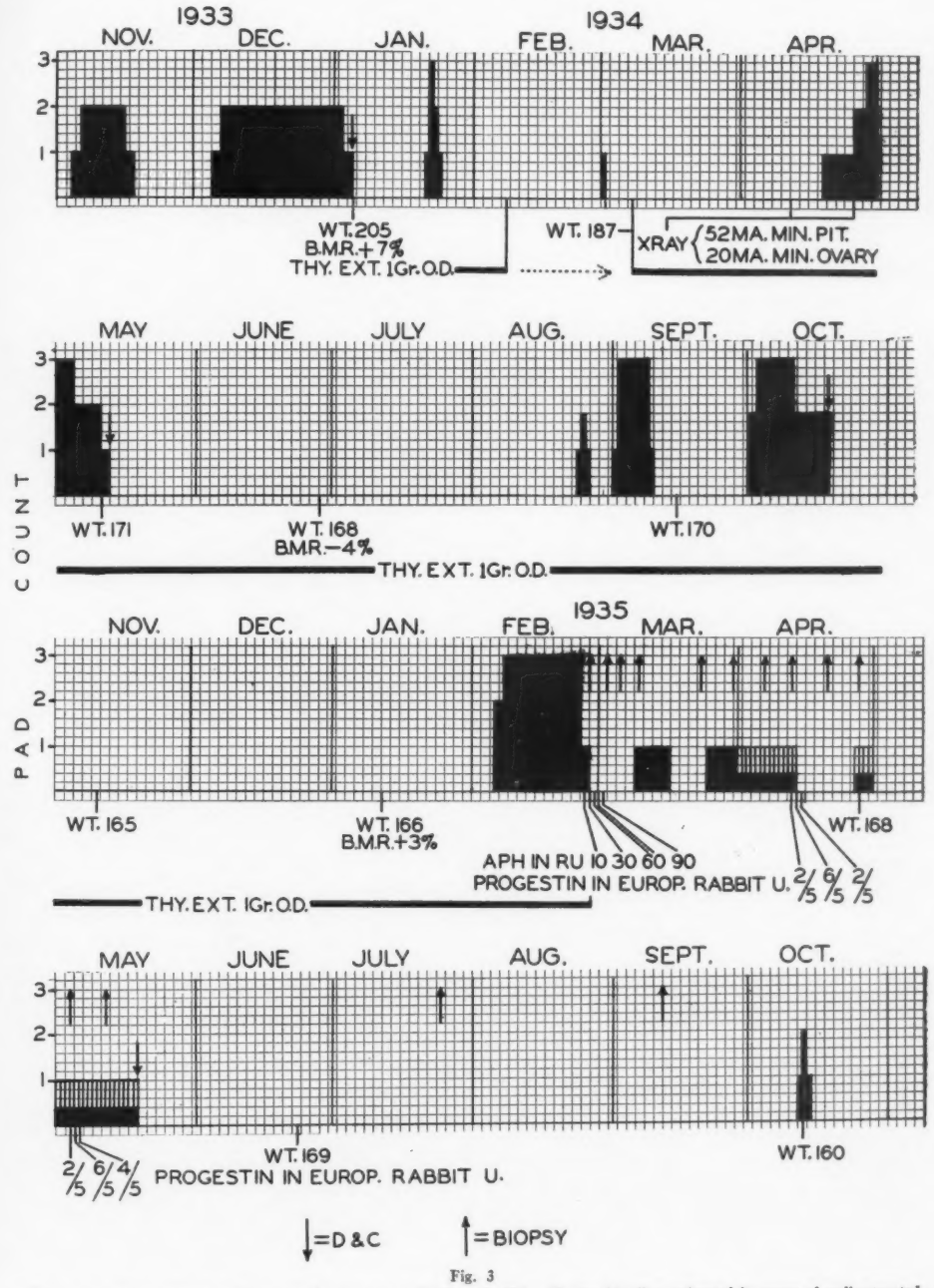


Fig. 3

Chart showing treatments and progress for two years (patient G. H.). Uterine bleeding estimated in terms of well-saturated heavy sanitary pads.

cessive uterine bleeding, there were very few patients benefited. The seven patients who had received snake venom therapy experienced checking of bleeding within seven to fourteen days and in six instances definite decrease in the bleeding was observed before the fifth day. No further excessive bleeding occurred during the course of treatment; however, three of these patients had prolonged excessive uterine hemorrhage following discontinuation of treatment and required in two instances hysterectomy and in another radium therapy. Thyroid therapy was ineffective in the two patients of this series. Bleeding stopped within four days after progestin therapy in the patient receiving the larger dose, but was not affected in the other instances. Of the 10 patients treated with APL/PU extracts, only two experienced decrease in the amount of the flow within five days. The flow ceased within five days in two of the six patients treated with APH.

Histopathologic study of endometria obtained

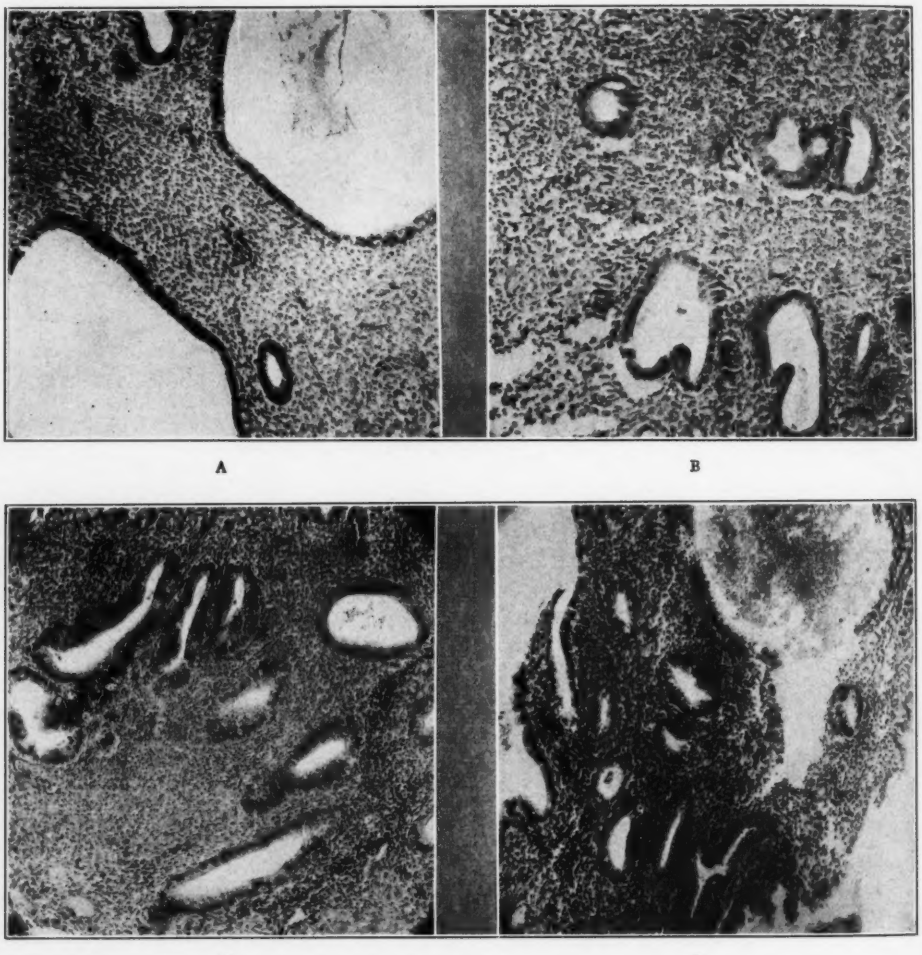
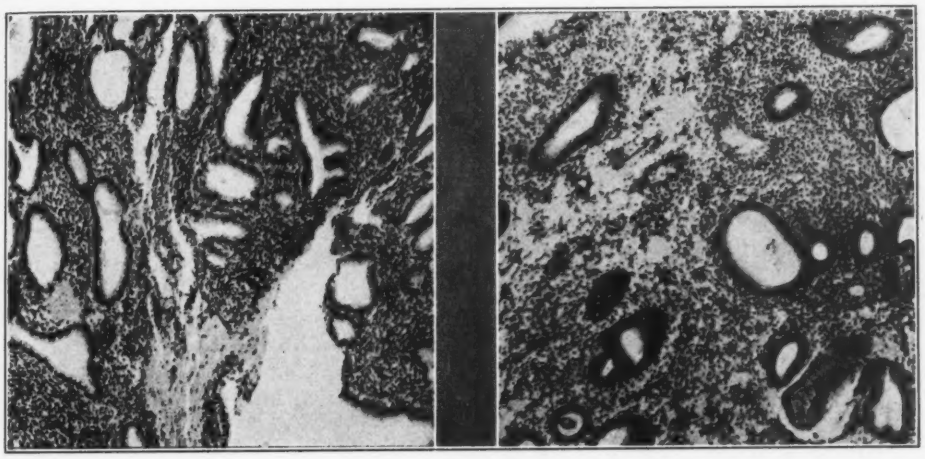


Fig. 4

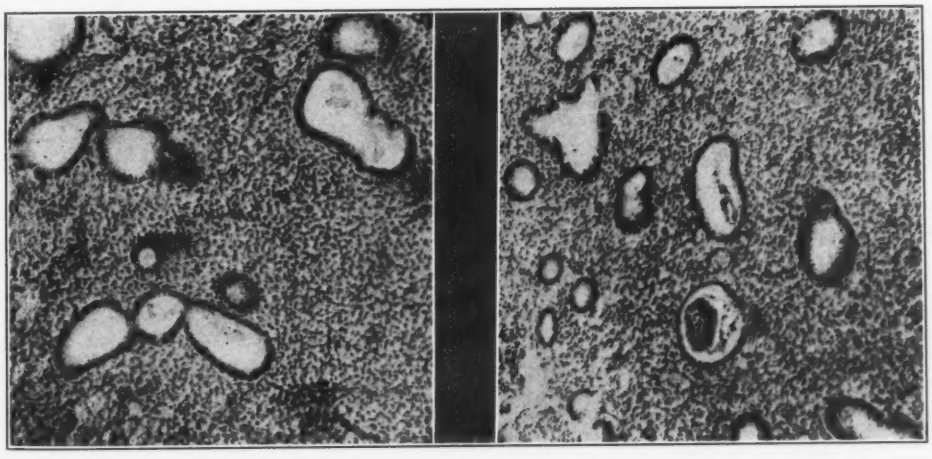
Endometria following therapy (see Fig. 3) (patient G. H.). (X110.)
(A) Bleeding 1/5, '34. (B) Bleeding 5/12, '34. After thyroid extract and radiation of ovaries and pituitary.
(C) Not bleeding: 3/2, '35. After "antuitrin," gonadotropic.
(D) Bleeding: 3/9, '35. After "antuitrin," gonadotropic.

from curettements and from biopsies revealed an apparent more orderly and uniform arrangement of the interval glands in a number of instances, but in only one specimen were glands of secretory progestational type observed. In this instance the patient (M. H.) had received injections of proluton (progestin) in 1 European rabbit unit dose daily for five days, the biopsy having been taken eight days after the first injection. One day following this biopsy an apparently normal menstrual period occurred which lasted for four days (*Fig. 7*).

The case of G. H., aged 16 years, is cited since it demonstrates refractiveness to many methods of attempted conservative therapy, including thyroid extract, low-dosage radiation of the ovaries and pituitary, APH extract and progestin. Weight reduction of 45 pounds likewise failed to benefit the uterine bleeding, which had been excessive, prolonged and irregular since menarche. The patient had required a curettement at 14 years of age. Physical examination revealed noth-



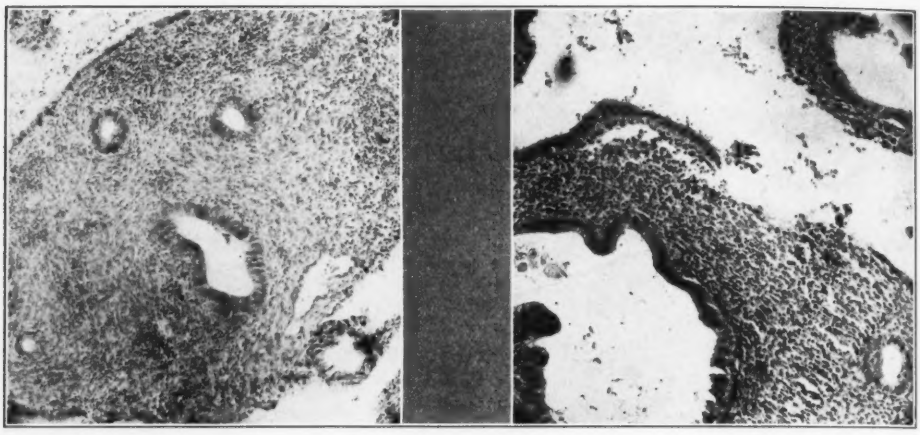
E F



G H

Fig. 5

Endometria following therapy (see Fig. 3) (patient G. H.). (X110.)
(E) Bleeding: 3/30, '35. After "antuitrin," gonadotropic.
(F) Bleeding: 4/12, '35. Before "proluton."
(G) Not bleeding: 4/20, '35. After "proluton." (H) Bleeding: 5/11, '35. After "proluton."

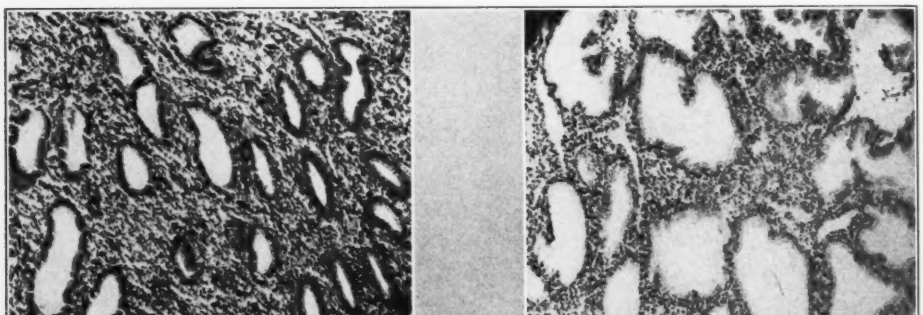


A B

Fig. 6

(A) Endometrium after "antuitrin S" (X110). Patient O. L., aged 22 years, had had irregular and excessive bleeding since menarche. Previous biopsy showed "swiss cheese" endometrial pattern. L. M. P. began July 6, 1935, bled profusely until curettage (specimen above) July 15, despite "antuitrin S" injections, 600 R. U. daily from July 9 to 14. Specimen shows slightly irregular interval glands with intact endometrial epithelium.

(B) Endometrium after "antuitrin gonadotropic" (X110). Patient V. M., aged 15 years, had had irregular, excessive uterine bleeding since menarche. Curettement on June 29, 1935, showed "swiss-cheese" pattern and temporarily controlled bleeding. Excessive bleeding occurred September 13, 1935. The patient returned for care October 10, 1935, with 54 per cent hemoglobin and red cells 2.65. She was treated by vaginal packing and "antuitrin gonadotropic," 80 R. U. daily from October 10 to 14, 1935, without decrease in profuse bleeding. Curettement October 15, 1935 (specimen above) and 400 mg./hr. radium. Specimen shows widely dilated late interval glands.



A B

Fig. 7

Endometrium before and after "proluton" (X110). The patient, M. H., aged 22, had had absolute irregularity of bleeding for four and a half years, becoming more profuse during the previous twelve months. Vaginal packing and curettement were necessary in December, 1934. The endometrium then showed "swiss-cheese" pattern. "Antuitrin S" therapy during the summer of 1935, was not effective. Recent bleeding spells have occurred as follows: September 14 to 22, saturating two to three napkins daily; October 12 to 23, using two to three well saturated pads daily; October 25 to November 3, slight spotting, requiring daily one pad about one-third saturated. Biopsy (A) October 29, 1935. "Proluton," 1 European rabbit unit daily from October 31 to November 4. Biopsy (B) November 8. An apparently normal menstrual period began November 9 and lasted until November 12.

ing abnormal except obesity with exaggerated pelvic and intertrochanteric fat padding (see *Fig. 2*). At her first visit her weight was 205 pounds; basal metabolic rate plus 7 per cent; hemoglobin 83 per cent; red cells 4,460,000. *Fig. 3* shows the course of uterine bleeding, treatments and progress of this patient over a period of two years. Endometrial studies following four curettements and 14 punch biopsies showed no progestational proliferation (*Figs. 4* and *5*).

DISCUSSION

The 27 patients who constitute the basis for this report were selected because they represented severe and long-standing cases of endometrial hyperplasia which had proven refractory to many of the conservative methods of treatment. As judged by an arbitrary clinical standard, the best results in this series were obtained from snake venom therapy. These beneficial results are undoubtedly only temporary in most instances.

Previous reports by one of us (Hamblen, 1933, 1935)[37 38] have shown no correction of the ovarian pathology in the younger group of patients with endometrial hyperplasia following treatments with the so-called luteinizing hormone from pregnancy urine (APL/PU). Similar studies are in progress to evaluate the effectiveness in this respect of injections of the gonadotropic hormone from the anterior lobe of the pituitary.

The studies of ovarian responses led us to expect to find no marked modification in the endometrial pathology following injections of principles which were supposed to act as ovarian stimulators or luteinizers. However, despite the lack of actual evidence of the correction of ovarian and endometrial abnormalities, clinical experiences of many indicate in some instances beneficial effects from such therapy. It seems likely that in these cases the action may be non-specific, perhaps affecting the clotting or bleeding mechanism or having some direct effect upon the walls of the small vessels of the endometrium.* Such an action is attributed to snake venom. Studies of the bleeding-clotting mechanism in these cases following various types of therapy are being carried on at present in our laboratories. McCullagh and Kearns (1935)[61] have studied the blood calcium and phosphorus levels in patients with functional menorrhagia following treatment with "antuitrin S" and conclude that, while there is a tendency towards a rise in some cases, in general variations in the concentrations of the sex hormones are not associated with variations in the level of serum calcium and phosphorus.

It has been hoped that progestin, when it became available for clinical use, would prove to have a direct action upon the pathologic endometrium in these cases. Observing a well formed progestational endometrium after progestin therapy is encouraging, especially when many negative results have been obtained. However, no conclusions are warranted from this single case. Subsequent studies of other patients may not demonstrate this effect, which may have resulted from an intercurrent ovulation. Further observations will be made upon endometria following progestin therapy. Since progestin is thought to act directly upon endometrium, it should be cautioned that its possible effect may prove only temporary since the ovarian disease would still persist.

*Geist, S. H.; and Spielman (Proc. Soc. Exper. Biol. & Med., **32**:353, 1934) were unable to find any significant effects upon erythrocytes, leukocytes, platelets or coagulation time following the treatment of six patients with functional bleeding with APL/PU extracts.

SUMMARY

Endometria obtained by curettement and punch biopsy from 27 patients varying in age from 14 to 34 years, who had been under observation for from two months to two years and whose treatments for hyperplasia of the endometrium included use of APL/PU extracts, gonadotropic extract of anterior lobe pituitary, thyroid extract, progestin, snake venom and low-dosage radiation of the ovaries and of pituitary, showed no evidence of progestational proliferation, except in one instance following progestin therapy.

We have been supplied generously with "antuitrin S" and "antuitrin-gonadotropic" by Dr. E. A. Sharp, of Parke, Davis & Co. "Proluton" has been made available through the courtesy of Dr. Erwin Schwenk, of Schering Corporation. Moccasin venom has been obtained through the kindness of Sharp & Dohme. We owe our thanks to other members of our staff who aided in the collection of the numerous biopsies and to our research technician, Miss Margaret Baptist, who has been of invaluable and constant help.

REFERENCES

1. Allen, E.; and Goldthorpe, H. C.: Study of Use of Parathormone in Control of Menstrual Bleeding. Amer. Jour. Obst. & Gyn., **17**:344-350, March, 1929.
2. Anspach, B. M.; and Hoffman, J.: Observations on Endocrine Diagnosis and Treatment of Amenorrhea and Functional Uterine Bleeding. Amer. Jour. Obst. & Gyn., **26**: 147-160, Aug., 1933.
3. Bakacs, G.: Gleichzeitiges Anwenden non Nebenschilddrusenhormon und Calcium bei krankhaften Blutungen der Gebarmutter. Zentralblatt f. Gynak., **57**:568-572, March, 1933.
4. Babes, A. A.: Etiology of Hyperplasia of Uterine Mucosa. Arch. f. Gynak., **122**:448-468, 1924.
5. Bartelmez, G. W.: Human Uterine Mucous Membrane During Menstruation. Amer. Jour. Obst. & Gyn., **21**:623-643, May, 1931.

6. Bartelmez, G. W.: Publication 443, Carnegie Institute, p. 183, 1933.
7. Bram, I.: Relation of Thyroid to Female Gonads: Resume of Observations in Over 13,000 Cases of Thyroid Disturbance. Med. Times and Long Island Med. Jour., **62**:10-13, Jan., 1334.
8. Brennecke: Zur Etiologie der "Endometritis fungosa:" Speciell der chronischen hyperplasierenden Endometritis Olshausen's. Arch. f. Gynak., **20**:445, 1882.
9. Burch, J. C.; Williams, W. L.; and Cunningham, R. S.: Etiology of Endometrial Hyperplasia. Surg., Gyn. & Obst., **53**:338-345, Sept., 1931.
10. Burch, J. C.; Williams, W. L.; Wolfe, J. M.; and Cunningham, R. S.: Hypophyseal-Ovarian Relationship: Quantitative Studies with Especial Reference to Hyperplasia of Endometrium. J.A.M.A., **97**:1859-1861, Dec., 1931.
11. Burch, J. C.; Wolfe, J. M.; and Cunningham, R. S.: Experiments on Endometrial Hyperplasia. Endocrinology, **16**: 541-546, Sept.-Oct., 1932.
12. Burch, J. C.; Phelps, D.; and Wolfe, J. M.: Endometrial Hyperplasia. Arch. Path., **17**:799-826, June, 1934.
13. Burch, J. C.: Personal Communication, 1935.
14. Burch, L. E.; and Burch, J. C.: Endometrial Hyperplasia: Review of Experimental Work. Amer. Jour. Obst. & Gyn., **25**:826-833, June, 1933.
15. Burnam, C. F.: in A. H. Curtis' Obstetrics and Gynecology. Philadelphia and London: W. B. Saunders Co., 1933.
16. Campbell, A. D.; and Collip, J. B.: On Clinical Use of Ovary-Stimulating Hormone of Placenta: Preliminary Report. Canad. Med. Assn. Jour., **22**:219-220, Feb., 1930.
17. Cooke, W. R.: Clinical Experiments with Thyroid in Gynecic Practice: Menorrhagia. Sou. Med. Jour., **24**:20-23, Jan., 1931.
18. Cooke, W. R.: Clinicopathologic Aspects of Endometriopathies. Texas State Jour. Med., **27**:844-847, April, 1932.
19. Corner, G. W.: Corpus Luteum Therapy. J.A.M.A., **104**: 1899-1901, May, 1935.
20. Cullen, T. S.: Address in Gynecology. Canad. Med. Assn. Jour., **3**:658, 1913.
21. Cullen, T. S.: Uterine Hemorrhage and Its Treatment. Canad. Med. Assn. Jour., **19**:411-420, Oct., 1928.
22. Driessen, L. F.: Endometritis, Folge abnormaler Menstruation, Ursache profuser Blutungen. Zentralblatt f. Gynak., **38**:618-622, 1914.
23. Elden, C. A.: Method of Study and Treatment of Menstrual Disturbances of Endocrine Origin. Amer. Jour. Obst. & Gyn., **28**:179-186, Aug., 1934.
24. Fluhmann, C. F.: Hyperplasia of the Endometrium and the Hormones of the Anterior Hypophysis and the Ovaries. Surg., Gyn. & Obst., **52**:1051, 1931.
25. Fluhmann, C. F.: Anterior Pituitary Hormone in Blood of Women: Preliminary Clinical Classification of Results in Non-Pregnant Individuals. Endocrinology, **15**:177-183, May-June, 1931.
26. Fluhmann, C. F.: Hyperplasia of Endometrium and Hormones of Anterior Hypophysis and Ovaries. Surg., Gyn. & Obst., **52**:1051-1068, June, 1931.
27. Ford, F. A.; and Drips, D. G.: Clinical and Experimental Studies of Low Dosage Irradiation of Ovaries and Hypophysis in Menstrual Disorders. Radiology, **12**:393-402, May, 1929.
28. Frank, R. T.: The Female Sex Hormone. Springfield, Ill.: Charles C. Thomas, publisher, 1929.
29. Frank, R. T.: Role of Female Sex Hormone. J.A.M.A., **97**:1852-1857, Dec., 1931.
30. Frank, R. T.: Selection of Appropriate Operation for Cure of Prolapse. Amer. Jour. Obst. & Gyn., **24**:574-582, Oct., 1932.
31. Frank, R. T.; Goldberger, M. A.; and Spielman, F.: Present Endocrine Diagnosis and Therapy: Critical Analysis Based on Hormone Studies in Female. J.A.M.A., **103**:393-402, Aug., 1934.
32. Gabrielianz, A.: Treatment of Functional Uterine Bleeding with Extract of Placenta. Amer. Jour. Obst. & Gyn., **28**: 262-263, Aug., 1934.
33. Geist, S. H.; and Spielman, F.: Therapeutic Value of Antuitrin-S in Menometrorrhagia. Amer. Jour. Obst. & Gyn., **29**:518-525, April, 1935.
34. Graves, W. P.: Some Observations on Etiology of Dysfunctional Uterine Bleeding. Amer. Jour. Obst. & Gyn., **20**: 500-518, Oct., 1930.
35. Hamblen, E. C.: Clinical Experience with Follicular and Hypophyseal Hormones: Preliminary Report. Endocrinology, **15**:184-194, May-June, 1931.
36. Hamblen, E. C.: Clinical Experience with Follicular and Anterior Pituitary Sex Hormones: Study of Results of Treatment in 120 Patients. Va. Med. Mo., **59**:464-474, Nov., 1932.
37. Hamblen, E. C.: Human Ovarian Responses to Extracts of Pregnancy Urine: Preliminary Report. Va. Med. Mo., **60**: 286, 1933.
38. Hamblen, E. C.: Results of Preoperative Administration of an Extract of Pregnancy Urine: A Study of the Ovaries and of the Endometria in Hyperplasia of the Endometrium Following Such Administrations. Endocrinology, **19**:169-180, 1935.
39. Hamblen, E. C.; and Ross, R. A.: A Study of Ovaries Following Preoperative Administration of an Extract of Pregnancy Urine. Amer. Jour. Obst. & Gyn., **31**:14, 1936.
40. Hintze, O.: Klinische Nachuntersuchung an 24 Fallen schwerer Hyperplasie der Korpusschleimhaut. Zentralblatt f. Gynak., **53**:2396-2495, Sept., 1929.
41. Hitschmann, F.; and Adler, L.: Der Baie der Uterusschleimhaut des Zeschlechtsreifen Weibes mit besonderer Berucksichtigung der Menstruation. Monatschr. f. Geburtsh. u. Gynak., **27**:1-82, 1908.
42. Hofbauer, J. I.: Hyperplasia endometrii pituitaria. Zentralblatt f. Gynak., **54**:2569-2573, Oct., 1930.
43. Hofbauer, J. I.: Concerning Etiology of Hyperplasia of Endometrium. Surg., Gyn. & Obst., **52**:222-227, Feb., 1931.
44. Johnstone, R. W.; Wiesner, B. P.; and Marshall, P. G.: Therapeutic Application of Gonadotropic Hormones ("Rho-factors"). Lancet, **2**:509-511, Sept., 1932.
45. Kaufmann, C.; and Bickel, L.: Uber die Behandlung genitaler Blutungen mit Corpus Luteum Hormon. Zentralblatt f. Gynak., **56**:1329-1333, May, 1932.
46. Kaufmann, C.: Echte menstruelle Blutung bei Kastrierten Frauen nach Zufuhr von Follikel-und Corpus luteum-Hormon. Klin. Wchnschr., **12**:217-218, Feb., 1933.
47. Keene, F. E.; and Payne, F. L.: Results of Radium Treatment in Functional Uterine Bleeding. Surg., Gyn. & Obst., **56**:322-329, Feb. (No. 2-A), 1933.
48. King, J. E.: Endometrial Hyperplasia and Its Relation to Endocrine Dysfunction. Amer. Jour. Obst. & Gyn., **26**: 582-587, Oct., 1933.
49. Klaften, E.: Intermittent and Prophylactic Insulin Therapy in Menorrhagias and Metrorrhagias. Zentralblatt f. Gynak., **59**:1512, 1935.
50. Klingler, H. H.; and Burch, J. C.: Suction in Obtaining Endometrial Biopsies. J.A.M.A., **99**:559-560, Aug., 1932.
51. Klingler, H. H.; and Burch, J. C.: Effect of Extracts of Urine of Pregnant Woman on Hyperplastic Endometrium. Amer. Jour. Obst. & Gyn., **26**:17-21, July, 1933.
52. Knab, F.: Beitrage zur Behandlung Ovariell bedingter Blutungen mit dem Hormon des Corpus Luteum. Zentralblatt f. Gynak., **57**:987-992, April, 1933.
53. Kretzschmar, N. R.: So-Called Essential Uterine Bleeding. Jour. Mich. Med. Soc., **32**:98-100, Feb., 1933.
54. Kurzrok, R.; Boylan, J.; Goldman, S.; and Creelman, M.: Estimation of Estrin and Follicle-Stimulating Hormone in Urine as Index of Therapy in Menstrual Dysfunction. Endocrinology, **16**:361-365, July-Aug., 1932.
55. Mazer, C.; and Hoffman, J.: On the Occurrence of Ovarian and Anterior Pituitary Hormones in the Urine of Pregnant Women. Amer. Jour. Obst. & Gyn., **18**:48, 1929.
56. Mazer, C.; and Goldstein, L.: Clinical Endocrinology of the Female. Philadelphia: W. B. Saunders Co., 1932.
57. Mazer, C.; and Ziserman, A. J.: Present Status of Female Sex Hormone Therapy. Med. Jour. & Rec., **135**:35-38, Jan., 1932.
58. Mazer, C.; and Goldstein, L.: Clinical Endocrinology of the Female. Philadelphia: W. B. Saunders Co., 1933.
59. Mazer, C.; and Katz, B. R.: Diagnosis and Treatment of Functional Uterine Bleeding. Sou. Med. Jour., **27**:13-20, Jan., 1934.
60. McClellan, G. S.; Phelps, D.; and Burch, J. C.: Endometrial Studies. Endocrinology, **19**:321-328, May-June, 1935.
61. McCullagh, E. P.; and Kearns, Jr., J. E.: The Relationship Between the Parathyroid Glands and Sex Hormones in Tetany. Endocrinology, **19**:532, 1935.
62. Mikulicz-Radecki, Von F. V.: Weitere Erfahrungen mit der Hysteroskopie, insbesondere beim Studium des Endometriums. Zentralblatt f. Gynak., **53**:258-264, Feb., 1929.
63. Meyer, R.: Arch. f. Gynak., **113**:259, 1920.
64. Mussey, R. D.; and Haines, S. F.: Amenorrhea and Oligomenorrhea Associated with Low Basal Metabolic Rates. Amer. Jour. Obst. & Gyn., **27**:404-408, March, 1934.
65. Novak, E.: Hyperplasia of the Endometrium. Amer. Jour. Obst. & Gyn., **75**:996-1001, 1917.
66. Novak, E.: Relation of Hyperplasia of Endometrium to the So-Called Functional Uterine Bleeding. J.A.M.A., **75**:292-297, 1920.
67. Novak, E.; and Martzloff, K. H.: Hyperplasia of Endometrium: Clinical and Pathological Study. Amer. Jour. Obst. & Gyn., **8**:385-411, Oct., 1924.
68. Novak, E.; and Hurd, G. B.: Use of Anterior Pituitary Luteinizing Substance in Treatment of Functional Uterine Bleeding. Amer. Jour. Obst. & Gyn., **22**:501-512, Oct., 1931.

69. Novak, E.: Etiology and Treatment of Functional Uterine Bleeding. Sou. Med. Jour., **25**:261-266, March, 1932.
70. Novak, E.: Observations on Gynecological Aspects of Endocrinology. Brit. Med. Jour., **2**:553-557, Sept., 1933.
71. Novak, E.: in Obstetrics and Gynecology, vol. 3, by A. H. Curtis. Philadelphia and London: W. B. Saunders Co., 1933.
72. Novak, E.: Letter: Menstruation and Ovulation. J.A.M.A., **102**:1322, 1934.
73. Novak, E.: Anterior Pituitary and Anterior Pituitary-Like Substances: Therapeutic Applications. J.A.M.A., **104**:998, March, 1935.
74. Novak, J.: Ueber die Behandlung der Menstruationsstorungen. Wien. klin. Wchnschr., **45**:1512-1515, 1932.
75. Olshausen, R.: Ueber chronische hyperplasierende Endometritis des Corpus uteri (Endometritis fungosa). Arch. f. Gynak., **8**:97, 1875.
76. Peck, S. M.: Attempts at Treatment of Hemorrhagic Diathesis by Injections of Snake Venom. Proc. Soc. Exper. Biol. & Med., **29**:519-581, 1932.
77. Peck, S. M.; and Goldberger, M. A.: Treatment of Uterine Bleeding with Snake Venom (Ancistrodon piscovorus). Amer. Jour. Obst. & Gyn., **25**:887-893, June, 1933.
78. Peck, S. M.; and Rosenthal, N.: Effect of Moccasin Snake Venom (Ancistrodon piscovorus) in Hemorrhagic Conditions. J.A.M.A., **104**:1066-1070, March, 1935.
79. Plass, E. D.: Observations on Functional Menstrual Disturbances of Adolescents. Amer. Jour. Obst. & Gyn., **21**: 205-210, Feb., 1931.
80. Pratt, J. P.: Ovarian Therapy. Endocrinology, **16**:45-51, Jan.-Feb., 1932.
81. Rock, J.: Clinical Trials with So-Called Female Sex Hormone. New Eng. Med. Jour., **208**:362-368, Feb., 1933.
82. Rock, J.: Changes in Endometrium After Female Sex Hormone Therapy: Consideration of Effect of Antuitrin-S in Human Subjects. Endocrinology, **19**:269-274, May-June, 1935.
83. Rossak, M.: Zur Anwendung des Kongorots bei gynakologischen Blutungen. Zentralblatt f. Gynak., **57**:219-220, Jan., 1933.
84. Schickele, G.; and Keller, R.: Die glandulare Hyperplasie der Uterusschleimhaut, irhe Beziehungen zu den Uterusblutungen. Arch. f. Gynak., **95**:586-608, 1933.
85. Schroder, R.: Anatomische Studium zur normalen und pathologischin Physiologie des Menstruationzyklus. Arch. f. Gynak., **27**:104, 1915.
86. Schroder, R.: in Halban, Joseph, and Seitz, Ludwig: Biologie und Pathologie des Weibes. Berlin: Urban and Schwarzenberg, **3**:921, 1924.
87. Seitz, A.: Arch. f. Gynak., **116**:252, 1922.
88. Shaw, Wilfred: Irregular Uterine Hemorrhage. Jour. Obst. & Gyn., Brit. Emp., **36**:1-69, 1929.
89. Shaw, W.: Letter: Ovulation and Menstruation. J.A.M.A., **102**:1961, 1934.
90. Shaw, W.: Ovulation and Menstruation. Brit. Med. Jour., **1**:7-10, Jan., 1934.
91. Siebke, Harold: Ergebnisse von Mengenbestimmungen des Sexualhormons: Sexualhormon im Blut. Zentralblatt f. Gynak., **53**:2450-2462, Sept., 1929.
92. Smith, G. Van S.; and Smith, O. W.: Role of Progestin in Female Reproductive Cycle. J.A.M.A., **97**:1857-1859, Dec., 1931.
93. Smith, G. V.; and Rock, J.: Dysfunctional Uterine Bleeding: Results in Treatment with Extracts of Urine of Pregnant Women. Surg., Gyn. & Obst., **57**:100-103, July, 1933.
94. Spivack, M.: Polycystic Ovaries in New Born and Early Infancy and Their Relation to Structure of Endometrium. Amer. Jour. Obst. & Gyn., **27**:157-173, Feb., 1934.
95. Stephan, R.: Zur frage der blutgerunung. Munch. med. Wochschr., **67**:992, 1920.
96. Taylor, H. C., Jr.: Endometrial Hyperplasia and Carcinoma of Body of Uterus. Amer. Jour. Obst. & Gyn., **23**:309-332, March, 1932.
97. Werner, A. A.; and Collier, W. D.: Effect of Theelin Injections on Castrated Woman, with Histologic Report. J.A.M.A., **100**:633-640, March, 1933.
98. Werner, Paul: Wie behandeltman amenorrhea im hypermenorrhea. Wien. klin. Wochschr., **44**:1413, 1931.
99. Witherspoon, J. T.: Interrelationship Between Ovarian Follicle Cysts, Hyperplasia of Endometrium and Fibromyomata: Possible Etiology of Uterine Fibroids. Surg., Gyn. & Obst., **56**:1026-1035, June, 1933.
100. Witherspoon, J. T.; and Butler, V.: Etiology of Uterine Fibroids with Special Reference to Frequency of Their Occurrence in Negro: Hypothesis. Surg., Gyn. & Obst., **58**: 57-61, Jan., 1934.
101. Wolfe, J. M.; Campbell, M.; and Burch, J. C.: Production of Experimental Endometrial Hyperplasia. Proc. Soc. Exper. Biol. & Med., **29**:1263-1265, June, 1932.
102. Zondek, B.: Polyhormonale Krankheitsbilder: Funktionelle Betrachtung gynakologischer Erkrankungen. Zentralblatt f. Gynak., **54**:1-7, Jan., 1930.
103. Zondek, B.: Hypophysennorderloppen. Arch. f. Gynak., **144**:133-164, 1930.
104. Zondek, B.: Primare polyhormonale Amenorrhae mit glandular - cystisch - hyperplastischer Schleimhaut by B. Zondek. Acta Obst. & Gyn., Scandinav., **13**:309, 1934.

DISCUSSION (*Abstract*)

Dr. John C. Burch, Nashville, Tenn.—I have listened with great interest to Dr. Hamblen's presentation of his results in the treatment of young women with endometrial hyperplasia. While I have not studied this phase of the question as extensively as he, my clinical impressions coincide with his results. As my own material has increased, I have gradually come to the conclusion that glandular cystic hyperplasia of the endometrium is not a disease entity, but a symptom of an underlying endocrinopathy. As a result of this conception, I have undertaken a study of hyperplasia and other menstrual disorders with the object of correlating the endometrial findings with the general state of the patient. While this study is in no way complete, it indicates that ovarian disorders, as expressed by the state of the endometrium, are of three degrees. In the first degree of ovarian failure there may be a normal or incompletely luteinized endometrium at the time of menstruation. In the second degree there is an aluteal endometrium of the same general type as seen in hyperplasia. In the third degree there is evidence of markedly diminished estrin secretion as expressed by the endometrial atrophy. Ovarian failure may be either primary or secondary. In the latter it is most often the result of a primary pituitary or a primary thyroid failure. Many of our therapeutic failures are the result of treating hyperplasia as an entity rather than as a symptom of an endocrinopathy. This point is of especial importance in the older group, as surgical and radiological treatments are designed to cure the symptom. The underlying condition is almost universally neglected and the patient, although cured of the symptom, is left with her important general condition untreated.

Dr. G. D. Royston, St. Louis, Mo.—Hyperplasia of the endometrium is generally considered to be due to altered ovarian function whereby there is a persistent follicular influence and an absence or lack of normal corpora lutea. It is a very common cause of excessive uterine bleeding, particularly in young girls and in those near the menopause. The patient's age, social condition, amount of bleeding and presence or absence of other pathological lesions must be considered in order to institute intelligent treatment.

If there are no demonstrable pelvic lesions, and in certain cases where such pelvic lesions can be found, a diagnostic curettage to remove all the endometrial tissue for microscopic examination is necessary for an accurate diagnosis. A biopsy is advisable in every case where the cervix is the least suspicious. Curettage sometimes cures, though more often bleeding recurs where hyperplasia is present, thus showing that the underlying cause still persists.

The ingenious method of Burch permits us to obtain in the office sufficient endometrium for examination one or two days before the date of expected menstruation to determine whether or not there is a secretory phase of this endometrium. Emil Novak states that he has never seen a well developed secretory phase of

endometrium that did not have a well developed corpus luteum.

The routine determination of basal metabolism is advisable. The next most valuable test for thyroid function is the determination of the basal pulse. Thyroid extract is administered where indicated and the patient is instructed to count her carotid pulse on awakening and before arising twice weekly, and enough thyroid is given to hold this basal pulse rate between seventy and eighty. Dr. Hamblen has shown that his good results from the use of snake venom are due to his treatment of the bleeding without removal of the underlying cause. Anterior pituitary-like sex hormone has given us encouraging results in a small number of patients treated.

According to Burnam, radium acts first upon the follicles, then upon the corpus luteum, primordial follicles and stroma in the order named; hence we can use the dose recommended by Keene, using from 200 to 1,200 millicuries, according to the patient's age. Such doses may be increased or repeated when indicated. In younger women the smaller dose is advisable, as it may be given without permanently destroying menstrual or reproductive function. Radium treatment gives the most satisfactory results in hyperplasia.

X-ray therapy may be given where bleeding is not too excessive. It is hardly a first choice because of the time necessary for its full effect. Hysterectomy is advisable in certain cases where it is imperative to check severe bleeding and when it is highly desirable to conserve the ovaries in younger women. It is also advisable in certain older women, neurotics, and where other pathological lesions require surgical treatment.

AN EVALUATION OF RADIOTHERAPY FOR CARCINOMA OF THE UTERUS AFTER FIFTEEN YEARS' EXPERIENCE AT THE WOMAN'S HOSPITAL*

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To estimate the value of any therapeutic measure for combating a disease, it is essential that one take cognizance of the cost the patient has to pay in danger to life, the suffering which must be endured, the duration of the convalescence, and the ultimate degree of health that may be obtained.

In evaluating a treatment for malignancy the first consideration is, what may be the permanent cure rate; the second is, what may we hope for as to prolongation of life if a permanent cure is not possible, and third, what degree of suffering the patient may have to endure and for how long.

In the treatment of carcinoma of the uterus we are limited at the present time to surgery, or radiotherapy, or a combination of the two.

In carcinoma of the cervix, radium associated with x-ray has largely displaced surgery alone in the majority of cancer clinics. This is due to the fact that the salvage rate of radiotherapy equals that of radical surgery without the high primary mortality incident to the Wertheim operation. The primary mortality of radium is less than 2 per cent, while that of the radical operation averages from 8 to 17 per cent. Also there is a general impression that the convalescent period with radium is without the same suffering and is much shorter than with surgery. This impression, however, is open to question, and a careful comparative study of post-irradiation convalescence with convalescence from radical surgery should be made to properly evaluate radiotherapy. In other words, "What price radium?"

In 1932, in a paper on the complications of radium therapy in gynecology, we called attention to the fact that in the enormous mass of literature that had been published up to that time, although the complications were mentioned, it was rare to find a detailed analysis of the subject, and very little had been written regarding the frequency of post-irradiation symptoms. Since that time a number of important contributions to the subject of complications have been made. Recent notable papers are by Palmer Findley, Newell and Crossen, T. E. Jones, H. G. Bugbee, Kirchhoff and Drenckhahn, Hamann and Goebel, Kessler and Schmidt, Brooke Bland, and others.

A sufficient period of time is necessary before one can form an opinion of real value of the treatment of this treacherous disease. After an experience of more than fifteen years in the use of radium in carcinoma of the uterus, we believe that a ten-year post-irradiation observation period gives us a more accurate evaluation of the curability of cancer by radiation than the usual five-year standard. We have published our series of five-year results in 1925, 1928, 1930, 1932 and 1934. In this last presentation before the 1934 meeting of the American College of Surgeons we also gave our ten-year results.

My associate, Dr. Nelson B. Sackett, presented an analysis of our cases before the Medical Society of the State of New York in May of this year which covered the period from February 15, 1919, to April 15, 1935. In this report special emphasis was laid on the health

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of the survivors as indicated by the complications observed.

Table I

FIVE-YEAR END RESULTS IN CARCINOMA OF CERVIX AT WOMAN'S HOSPITAL

Patients Seen from February 15, 1919, to April 15, 1930

Schmitz Class	All Classes	I	II	III	IV	V	I and II Early	III, IV and V Late
Total seen	493	10	89	345	47	2	99	394
Irradiated	474	10	89	345	28	2	99	375
Untreated	19	0	0	0	19	0	0	19
Living 5 years	127	7	47	73	0	0	54	73
Absolute survival per cent	25.8	70.0	52.8	21.1	0	0	54.5	18.5
Relative survival per cent	25.8	70.0	52.8	21.1	0	0	54.5	19.5

Untraced, counted dead from cancer, 13 (2.7 per cent).

Sackett's analysis showed that from February 15, 1919, to April 15, 1930, we saw in the clinic 493 patients with carcinoma of the cervix in all stages of the disease. Ninety-nine were classed as early (I and II) and 394 as late (III, IV and V). Of these 474 were irradiated, while 19 were too far advanced for treatment. One hundred and twenty-seven of all classes survived for five years, which was an absolute survival of 25.76 per cent. The relative survival rate (treated cases) was 26.8 per cent. Of these survivors 54, or 54.5 per cent, were early cases, and 73, or 19.5 per cent, were in the advanced group. There were 13 untraced cases counted dead of cancer, 2.7 per cent. This table shows that one in four of all stages, and one in two with the disease limited to the cervix, and seven out of ten very early cases have had the disease arrested for at least five years following radiotherapy in our clinic.

Table II

TEN-YEAR END RESULTS IN CARCINOMA OF CERVIX AT WOMAN'S HOSPITAL

Patients Seen from February 15, 1919, to April 15, 1925

Schmitz Class	All Classes	I	II	III	IV	I and II Early	III and IV Late
Total seen	254	3	61	172	18	64	190
Irradiated	247	3	61	172	11	64	183
Untreated	7	0	0	0	7	0	7
Living 10 years	42	2	24	16	0	26	16
Absolute survival per cent	16.5	66.6	39.3	9.3	0	40.6	8.4
Relative survival per cent	17.0	66.6	39.3	9.3	0	40.6	8.7

Untraced, counted dead from cancer, 12 (4.9 per cent).

The ten-year study of the patients who first came to the clinic during the period from February 15, 1919, to April 15, 1925, shows there were 254 of all degrees of the disease, of whom 64 were early and 190 advanced. In 7 of these the carcinoma had progressed too far for treatment. Of the 247 treated, 42 were alive, 26 of the early and 16 of the late group. This gives an absolute survival rate of 16.5 per cent and a relative rate of 17 per cent. Twelve (4.9 per cent) were untraced and counted dead of cancer. Thus one out of six of all this group, two out of five in the early, and two out of three in the very early stages of the disease have survived ten years or longer.

Table III

TEN-YEAR END RESULTS IN CARCINOMA OF CERVIX

Patients Seen from February 15, 1919, to May 15, 1924

		5-Year Survival as of May 15, 1929			10-Year Survival as of May 15, 1934		
		Living	Survival Rate Per Cent	Untraced	Living	Survival Rate Per Cent	Untraced
Total seen	208	53	25.48 (abs.)	9	37	17.79 (abs.)	11
Total treated	202	53	26.24 (rel.)	4.45 Per Ct.	37	18.31 (rel.)	5.45 Per Ct.
Untreated	6						

Table III gives the ten-year end results from 1919 to 1934. This table shows that 70 per cent of the patients surviving five years have lived ten years or longer in spite of the lowered life expectancy of their respective age groups.

In the report we gave in October, 1934, the ten-year results showed 208 cases seen and 202 treated with 53 salvaged, or an absolute survival rate of 17.7 per cent, and a relative rate of 18.31 per cent with 11 cases (5.45 per cent) untraced. This group shows that 70 per cent of patients surviving five years have lived ten years or longer in spite of the lowered life expectancy of their respective age groups. However, we have had several patients free of symptoms ten years or more who have ultimately died of cancer of the uterus, or in whom the disease could not be definitely excluded.

In these series high voltage x-ray therapy was not available. From 1933 x-ray has been an adjuvant to the radium therapy employed and we hope our figures will show improvement in 1937.

In 688 cases we have seen 50, or 7.3 per cent, of carcinoma in the cervix stump following supravaginal hysterectomy. Of these 15 have

Table IV

INCIDENCE AND CURABILITY BY IRRADIATION OF CARCINOMA OF CERVIX FOLLOWING SUPRAVAGINAL HYSTERECTOMY*

Schmitz Class	I	II	III	IV	V	All Classes	Early Per Cent	Late Per Cent
Total seen	4	9	31	5	1	50	26	74
All treated per cent	8	18	62	10	2	100		

Incidence: 50 in 688 cases seen, or 7.3 per cent.
Incidence: 50 in 664 cases treated, or 7.5 per cent.

Series	Total Seen	Irradiated	Living 5 Years	Living 10 Years	Survival Rate Abs. and Rel. Per Cent
1919 to May 15, 1930	31	31	15	—	48.4 at 5 yrs.
1919 to May 15, 1925	16	16	7	4	25.0 at 10 yrs.

*Without regard to time elapsing between hysterectomy and first irradiation. This interval varied from two weeks to 18 years; it was three years or less in 24 cases, four years or more in 23 cases.

Table V

COMPLICATIONS IN CARCINOMA OF CERVIX UTERI TREATED BY IRRADIATION

Cases Seen at Woman's Hospital February, 1919-April 15, 1935*

Complications	260 Cases Seen Before 5/15/25	238 Cases Seen 5/15/25 to 5/15/30	190 Cases Seen 5/15/30 to 5/1/35	All 688 Cases 1919 to 1935	
				No.	Per Ct.
Pyometra	15	28	12	55	7.9
Peritonitis and sepsis	2	4	4	10	1.5
Intestinal obstruction	2	11	12	25	3.6
Fistula, patients	16	27	17	60	8.7
Fistulae, number	20	34	19	73	10.6
Hemorrhage, severe	24	31	34	89	12.9
Rectal disorders	4	14	24	42	6.1
Bladder and urethra	12	23	32	67	9.8
Upper urinary tract dis.	11	12	16	39	5.6
Upper G. I. tract dis.	4	5	5	14	2.0
Blood-lymphatic obst.	8	11	10	29	4.2
Nervous symptoms, pain, etc.	5	5	16	26	3.7

*Complications not noted uniformly in earlier cases, in hopeless cases, and cases lost in follow-up. Many duplications as one complication precedes or is an early stage of another.

lived five years, or 48.4 per cent, and 7 have lived ten years, or 25 per cent. The time elapsing between the hysterectomy and the irradiation varied from two weeks to eighteen years. It was three years or less in 24 cases, and four years or more in 23 cases.

In these stump cases, there is a greater danger of vesicovaginal fistula as a result of the treatment, as the bladder then lies on top of the cervix at the site of the amputation, where it will come in direct contact with the radium tube placed in the cervical canal. In our patients the incidence of hemorrhage and of fistula was increased in these cases.

An estimation of post-irradiation mortality and morbidity is naturally confused and complicated by the ravages of the disease itself. As three-fourths of all cases seen do not survive the five-year period, it is reasonable to assume that the cancer is responsible for the mortality and much of the morbidity rather than the irradiation.

An approximate indication of the incidence of complications in this series of 688 cases is shown in Table V, although it is not possible to differentiate those complications due to the disease from those due to the radiotherapy. Many of course may be rightly attributed to both factors. In this table cases seen during three five-year periods are given and show that pyometra was observed in 7.9 per cent, peritonitis and sepsis in 1.5 per cent, intestinal obstruction in 3.6 per cent, patients developing fistulae 8.7 per cent, severe hemorrhage 12.9 per cent, rectal disorders 6.1 per cent, bladder and urethra symptoms 9.8 per cent, upper urinary tract involved 5.6 per cent, upper gastro-intestinal symptoms 2 per cent, blood and lymphatic obstruction 4.2 per cent, and nervous disorders, pain and so on, 3.7 per cent.

In the earlier cases, hopeless cases and cases lost in the follow-up, complications were not always accurately recorded. There are also many duplications, as one complication precedes or is an early stage of another. This gives us an index of the price these patients had to pay for radium therapy. Except for hemorrhage, each of these complications occurred in less than 10 per cent of the cases.

In Table VI the complications occurring in those that survived five years and those that lived ten years or longer are given.

In the 127 cases that were salvaged for five years the incidence of pyometra was 7.1 per cent, peritonitis and sepsis 1.6 per cent, intestinal obstruction 1.6 per cent, patients developing fistulae 8.7 per cent, severe hemorrhage 3.9 per cent, rectal disorders 3.9 per cent, bladder and urethra symptoms 8.7 per cent, upper urinary tract disease 5.5 per cent, upper gastro-intestinal symptoms 3.2 per cent, blood lymphatic obstruction 5.5 per cent, and nervous symptoms, pain and so on, 0.8 per cent.

Table VI

COMPLICATIONS IN CARCINOMA OF CERVIX UTERI TREATED BY IRRADIATION

Cases Surviving as of April 15, 1935

Complication	Survivors Over 10 Years, 42 Cases to 5/15/25 No. and Per Cent		All 688 Cases 1919 to 1935 Per Cent	Total 5-Year Survivors 127 Cases 1919 to 5/15/30. No. and Per Cent	
Pyometra	4	9.5+	7.9	9	7.1—
Peritonitis and sepsis	0—		1.5	2.	1.6+
Intestinal obst.	0—		3.6	2	1.6—
Fistula, patients	3	7.1	8.7	11	8.7=
Fistulae, number	5	11.9+	10.6	17	13.4+
Hemorrhage, severe	3	7.1—	12.9	5	3.9—
Rectal disorders	0—		6.1	5	3.9—
Bladder and urethra	2	4.8—	9.8	11	8.7—
Upper urinary tract dis.	2	4.8—	5.6	7	5.5—
Upper G. I. tract dis.	1	2.4—	2.0	4	3.2+
Blood-lymphatic obst.	4	9.5+	4.2	7	5.5+
Nervous symptoms, pain, etc.	0—		3.7	1	0.8—

Plus (+) sign means that complication is more frequent in survivors than in whole group.
Minus (—) sign means that complication is less frequent in survivors than in whole group.

In the 42 patients who survived ten years or longer pyometra occurred in 9.5 per cent, there were no cases with peritonitis and sepsis, and no cases of intestinal obstruction. Fistula was a complication in 7.1 per cent and severe hemorrhage in 7.1 per cent. There were no rectal disorders of moment. The bladder and urethra were affected in 4.8 per cent, upper urinary tract in 4.8 per cent, upper gastro-intestinal tract in 2.4 per cent, blood lymphatic obstruction in 9.5 per cent, and there was none with nervous symptoms or pain.

This demonstrates that the majority of complications are less frequent in the patients destined to survive, and that many of the complications occurring in this group are of a transitory nature.

All the untreated cases die of the disease and the complications of the various organs involved are of course due to the carcinoma. In the treated cases that die the complications often appear shortly before death and in many they are also due to the disease itself and not to the radiotherapy. The development of complications, then, we must always regard as an unfavorable sign, as in many cases it is an indication of a probable extension of the carcinoma. However, we have been agreeably surprised in some instances to see a patient whom we had considered in a hopeless condition report to the follow-up clinic some months later restored to health with an arrest of the disease. These patients undoubtedly were suffering from late radium reactions and not from the progress of the carcinoma. We have learned therefore to reserve judgment on the outcome of these hopeless cases.

As an illustration we give here a brief abstract of the cases of some patients whom we had dismissed from the clinic as hopeless, and whom we had placed in hospitals for incurables, as dying of cancer:

Mrs. B. came to us with extensive carcinoma of the cervix, Class III, in June, 1919. Her previous weight was 219 pounds. She had three applications of radium, the last in March, 1920, developed vesicovaginal and rectovaginal fistulae, and was admitted to the House of Calvary in June, 1920, weighing 100 pounds, as having but a short time to live. She returned to us in July, 1921, with the rectovaginal fistula healed, feeling well and weighing 233 pounds. She has a vesicovaginal fistula, but fortunately it is situated high up, so that by frequent emptying of the bladder she is fairly comfortable and is strong and able to do her daily work. She is well today after sixteen years.

Miss M. J., aged 30, came under my observation in February, 1927, with carcinoma of cervix Class III, squamous cell, Group I. She was given 4,200 mg. hours. She had considerable slough and did not respond well, became cachectic, lost weight and developed a vesicovaginal fistula in the anterior vault 2 cm. in diameter. She entered the House of Calvary as a hopeless case, but to our astonishment returned to our follow-up clinic in December, 1927, with no evidence of the disease and feeling perfectly well except for the fistula. I successfully operated upon the fistula in February, 1928, and she has remained in excellent health to date, nearly nine years.

Mrs. E. O., aged 27, came to the clinic in July, 1926, with a carcinoma of the cervix, Class III, Group I. She was radiated, but did not respond well, and as she seemed in a hopeless condition, she entered the House of Calvary in January, 1927. She returned to us in September, 1927, apparently free from carcinoma and having gained twenty pounds in weight. In February, 1930, she developed a pelvic abscess which resulted in a fecal fistula between the upper sigmoid and the vaginal vault. The fistula, however, was small and did not trouble her greatly unless her bowels were loose. In February, 1932, she developed an acute cellulitis over the center of the posterior surface of the sacrum which we felt certain was due to bony metastasis, although the x-rays were negative. On March 8, 1932, I opened this abscess and next day a fecal discharge was in evidence. X-ray studies showed that this sinus ran through the sarcosciatic notch to the original fistula, which thus discharged through the vagina and through the back over the sacrum. On March 29, 1932, I made a temporary colostomy and the sacral sinus has closed and the vaginal sinus nearly so. There is no evidence of carcinoma to be determined and she seems perfectly well over nine years after her original radiation. It is

our intention to close the colostomy should the vaginal fistula heal.

Mrs. P., aged 33, with squamous carcinoma (Group II) of the cervix, Schmitz III, L. N. II, was radiated October 9, 1933, with 3,600 mg. hours and two series of high voltage x-ray. She developed complications of phlebitis, cystitis and proctitis. X-ray studies showed narrowing of the sigmoid, which we now know to have been a part of the pelvic inflammatory condition. She was admitted to the Home for Incurables on March 12, 1934, suffering great pain with marked cachexia and emaciation. On October 30, 1935, she returned to our clinic apparently free from carcinoma and feeling well, having gained forty-three pounds.

The duration of time between the radiation therapy and the recovery in these four cases was: Miss J. one year, Mrs. O. one and one-half years, Mrs. B. and Mrs. P. two years. These were probably cases of late reactions.

Dr. T. E. Jones, of the Cleveland Clinic, called attention in 1932 to the possibility of intestinal injury by radiation therapy that often months or years later may produce symptoms of obstruction and pain due to benign adhesions that can easily be confused with a recurrence of the malignancy, and that the detection and proper surgical treatment of this complication will save the lives of such patients, who otherwise would be regarded as having hopeless malignancy. He has reported seven such cases occurring in 520 patients with cervical carcinoma, in which strictures were demonstrated as a result of benign adhesions; six of these were corrected by appropriate surgery with five recoveries.

It is obvious that patients who present such late symptoms should have the benefit of an x-ray diagnosis wherever possible, and an exploratory laparotomy should be performed. If the lesion is benign it may be corrected. If malignancy is present it may be possible to remove invaded lymph nodes and to perform a sympathectomy for the relief of pain. That there is a definite danger of injurying the intestine by the application of radium there can be no doubt, especially in cases where there are adherent loops of gut to the uterus or cul-de-sac of Douglas. Intestinal obstruction occurred in twenty-five of our series, and was the cause of death in nine. Five of these were operated upon with three deaths from postoperative peritonitis, and four died without operation. Carcinoma was present in nine of eleven patients who had an operation or autopsy. Seven patients were relieved by operation and two are still alive three and two and a half years after laparotomy.

Upper urinary tract disease, which occurred in 39 of the 688 cases, was usually a late development and generally due to obstruction of the ureter with resulting infection, hydro and pyonephrosis, or destruction of the kidney. The ureteral obstruction was demonstrated by catheterization in these cases and was usually 4 cm. from the orifice.

The action of radium which produces a proliferation of connective tissue with subsequent contraction is responsible for the complication in many cases, due to the proximity of the ureters to the sides of the cervix as they pass through the base of the broad ligaments, although the invasion of the carcinoma into the same region is a frequent cause. Dr. Bugbee, of my staff, has reported six cases of ureteral occlusion following irradiation, in which a nephrectomy was necessary. The time which elapsed from the radiotherapy to the nephrectomy varied from five months to nine years. We believe that in the follow-up of these patients, urinary disturbances should be watched for and the patient promptly cystoscoped, as the early discovery of ureteral stricture may allow of its being relieved by dilatation, or if necessary a nephrectomy may be done. The complication of a unilateral or bilateral ureteral occlusion following radiotherapy for carcinoma of the cervix is a possibility that must always be kept in mind.

This contraction of connective tissue in the pelvis as a result of irradiation may be a cause of obstruction to the venous and lymphatic circulation of the lower extremities, as may extension of the cancer. We observed phlebitis in five cases and obstructive lymphedema in twenty-three cases. In one-half of these the disorder was bilateral and it usually progressed as the cancer developed to a fatal termination. In the four cases in which the complication subsided, we believe it was due to the inflammatory changes produced by the irradiation.

It is a question as to whether the very high voltages in x-ray therapy which have been recently advocated may be a potential danger in increasing the incidence of intestinal adhesions with resulting stricture, and causing ureteral occlusion, or obstruction to the venous and lymphatic circulation.

Late vesical symptoms of frequency, dysuria and hematuria are not infrequently the result of

ulcerations of the bladder mucosa caused by the radium application and are not always due to the invasion of the carcinoma. We have had several cases in which the cystoscopic report stated that the ulceration was carcinomatous, which ultimately entirely recovered. Sixty of our series developed vaginal fistulae. Twenty-two per cent of the patients with the disease too far advanced for treatment developed fistula, and the disease had extended beyond the cervix in 85 per cent of those who subsequently had these lesions. It is difficult to tell whether the fistula is a result of the disease or the therapy, or both.

Pyometra and hematometra were observed in fifty-five of our cases and this may be a late complication following stenosis of the cervical canal following the irradiation.

We have observed in our follow-up many instances of an apparent extension of the carcinoma as evidenced by increase in the size of the uterus and marked pelvic pain and temperature that on investigation proved to be a retention of purulent or bloody fluid in the body of the uterus as a result of stenosis of the canal following the contraction from irradiation. The passage of a sound will at once clear up the diagnosis and an occasional passage of dilators will suffice to correct this complication. We have several instances of patients to whom a hopeless prognosis was given who are now alive and well, as the trouble was due to this condition and not to an extension of the disease. Undoubtedly the automatic evacuation of a pyometra accounts for the sudden improvement in the toxic condition of some of these patients whom we have believed to be hopeless cases.

Severe hemorrhage occurred in 89 of these 688 patients and was the most frequent complication. We must expect the possibility of hemorrhage at the time of the separation of the slough resulting from irradiation. Usually this is only slight, but occasionally it may be excessive, requiring prompt packing and even transfusion.

Our incidence of peritonitis and sepsis lighted up by the irradiation was low, only 1.5 per cent. In some clinics it has been quite high. Gosset and Wallon, in 1934, report a 7 per cent mortality rate in their cases treated with radium at the Salpetriére, in which infection played the leading role. Kirchhoff and Drenckhahn, in 1934, report 924 cases of carcinoma of the cervix observed in the Kiel Frauenklinik during a period of eleven years in which they compare the morbidity and mortality after irradiation and surgery. Four hundred and fifty-nine patients were treated by radium and 401 were operated upon. The primary mortality of the irradiated group was 3.9 per cent, embolism, peritonitis, sepsis, uremia, hemorrhage and myocardial insufficiency being the causes. Forty per cent had complications. There were minor reactions in 24.4 per cent, and major complications occurred in 9.2 per cent. The cases treated by surgery had a primary mortality of 8.72 per cent and the late complications occurred in the same relative proportion.

Carcinoma of the fundus occurs in about 10 per cent of uterine cancer and since January, 1919, 134 such patients have been admitted to the hospital. Ninety-seven of these have been seen in our clinic, 92 of whom have been treated, 61 by irradiation alone, 25 by radium and hysterectomy, and 6 by hysterectomy alone. As this type of the disease is more frequent in the later decades of life, many are poor operative risks on account of old age, obesity, cardiovascular disease, deficient renal function, or diabetes. These complications were present in more than 50 per cent of our cases so that radiotherapy alone had to be relied upon. An estimate of the complications in these patients is very difficult to make because of the associated diseases and physical condition present. An analysis of this group is now being made, but as yet is not completed.

CONCLUSIONS

In this communication we have attempted to call attention to the fact that the complications associated with radiotherapy are considerable, although the great majority are of minor degree and transitory. However, there still remains approximately one-third who have major complications. It is of course difficult to differentiate those that are due to the cancer and those that are the result of the irradiation, but this study of 688 cases indicates that except for hemorrhage each complication occurs in less than 10 per cent of the patients, and that most of them are less frequent in the patients destined to survive as shown in our five- and ten-year series. We cannot always avoid some of these complications, as they occur in the most experienced

hands; but they can be materially reduced in number, if the action of radium on the tissues is understood and meticulous care is taken in following the essential details of the preliminary treatment and technic of application. A comparative study of the late complications occurring after surgery and after radiotherapy should be made. We know that complications may occur some years after irradiation that are not necessarily due to a recurrence of the disease. If such complications do not occur so frequently in surgery we should know it.

We have endeavored to emphasize the serious nature of the major troubles that may occur late in the course of the convalescence even though the patient may ultimately recover from the carcinoma, and that this is the price the patient has to pay for salvage and palliation by radiotherapy.

REFERENCES

Findley: Trans. Amer. Assn. Obst., Gyn. & Abd. Surgeons, p. 111, 1933.
Idem: Canad. Med. Assn. Jour., **32**:154, 1935.
Newell and Crossen: Surg., Gyn. & Obst., **60**:763, April, 1935.
Jones: Surg., Gyn. & Obst., **59**:644, 1934.
Idem: J.A.M.A., **103**:1678, 1934.
Idem: Amer. Jour. Obst. & Gyn., **29**:309 (March) 1935.
Bugbee: Jour. Urol., **32**:439, 1934.
Kirchhoff and Drenckhahn: Strahlentherapic, **50**:428, 1934.
Hamann and Drenckhahn: Zentralblatt fur Gyn., **59**:677 (March) 1935.
Kessler and Schmidt: Strahlentherapic, **44**:349, 1932.
Bland: Amer. Jour. Obst. & Gyn., **17**:528 (April) 1929.
Ward: Amer. Jour. Obst. & Gyn., **25**:1 (Jan.) 1933.
Ward and Farrar: J.A.M.A., **85**:159 (July) 1925.
Idem: Amer. Jour. Obst. & Gyn., **11**:— (April) 1926.
Idem: J.A.M.A., **91**:296 (Aug.) 1926.
Ward: Amer. Jour. Obst. & Gyn., **17**:— (Jan.) 1929.
Ward and Farrar: Surg., Gyn. & Obst., **52**:558 (Feb.) 1931.
Ward: Surg., Gyn. & Obst., **56**:434 (Feb.) 1933.
Ward and Sackett: Surg., Gyn. & Obst., **60**:495 (Feb.) 1935.
Sackett: N. Y. State Jour. Med., **35**:1153 (Nov.) 1935.
Gosset and Wallon: Arch. d'electric Med., **42**:279, 1934.

DISCUSSION (*Abstract*)

Dr. Fred J. Taussig, St. Louis, Mo.—The splendid results obtained by Dr. Ward and the careful and complete analysis of the postradium complications is deserving of special praise. We at the Barnard Free Skin and Cancer Hospital can show no record of cure comparing to his. It must, however, be borne in mind that every cancer hospital labors under difficulty in comparable results with those of a general hospital because of the larger number of hopeless cases referred to it. We have had our share of complications, but these have fortunately grown steadily less in the past years and particularly in the last one and a half years.

There has been marked improvement, due, I believe, to the use of a gold capsule 2 millimeters in diameter as a filter instead of the brass capsule formerly employed. The irritation from the rays is, therefore, completely excluded, the resulting reactions are less pronounced and healing occurs more rapidly. Reradiation is responsible for many of these complications.

Sometimes a fistula is a blessing in disguise, particularly the rectovaginal type, since it removes the intestinal stagnation responsible for much of the patient's pain and toxemia. Operating these fistulas is by no means as hopeless as would appear after inspecting the scarred walls of the vagina. I have recently had considerable success in cases of vesicovaginal fistula.

Finally, I should like to say that in the Group I cases, the early type limited to a portion of the cervix, our operative results have been so satisfactory that we still prefer operation to radiation. I am particularly struck with the fact that after surgery there are fewer late recurrences between five and ten years than after radiation.

In a certain percentage of the Group II cases in which a hysterectomy is inadvisable but the patient presents no operative contraindications, I have advised removal of the tributary lymph nodes. This operation of iliac lymphadenectomy which I have done for the past five years is not a serious procedure if limited to the Group II cases. My first patient operated upon by this method in October, 1930, with cancer present in the lymph nodes, has just passed her five years free of recurrence.

Lymph node metastasis is notoriously resistant to irradiation treatment and our only hope, therefore, lies in node resection. The value of this procedure is still undetermined, but results thus far are encouraging.

Dr. M. Y. Dabney, Birmingham, Ala.—Two complications of irradiation of uterine carcinoma demand especial consideration, pyometra and ureteral stricture, including its sequela, upper urinary tract disease, because much can be done to prevent or alleviate them. In the case of pyometra, heavy intra-uterine irradiation of the fundus to cause complete obliteration of the upper uterine canal should never be neglected. The tendency in some quarters is to confine irradiation almost exclusively to the cervix in carcinoma of cervical origin. If this latter course be pursued, pyometra will be encouraged, because all external carcinoma is potentially infected.

As to ureteral obstruction due to the invasion of the ureters by the carcinoma as well as by the deposition of fibrous tissue about them following irradiation, statistics of incidence may be rather inaccurate. The symptoms complained of often are too vague and varied to enable the gynecologist or radiologist to recognize their urologic origin. Probably as many as one-third of the five-year or longer "cures" have some ureteral contraction due to irradiation; and the number may be reduced greatly by routine cystoscopic study four to six months after irradiation, and by dilating the ureters to the size of a number 14 (French) catheter repeatedly at six-month intervals. It is easier to prevent post-irradiation stricture than to dilate such an obstruction, for some of them cannot be dilated at all after they have existed for any length of time. It is better to prevent this complication than to be forced to do a nephrectomy or a Coffey ureterosigmoidal anastomosis at a later date in the very intractable case.

Dr. George Gellhorn, St. Louis, Mo.—From what you have heard today and from what you have read these past five or ten years, you may have gotten the impression that radiotherapy is the only available or desirable form of treatment for cancer of the cervix.

Such an impression would, however, be faulty. A general surgeon would scorn the idea of giving up operating for early cancer of the breast, the stomach or the lip. He might consider radium or x-rays as valuable adjuncts or rely on them altogether in more advanced cases. There is no essential difference between cancer of the cervix and that of those other organs. It is true that the uterus is less easily approachable, and that the two special methods designed for removal of the cancerous uterus, methods which are quite different from ordinary hysterectomies, present considerable technical difficulties. But such difficulties exist only to be overcome. We ourselves are the best proof of this seemingly bold statement. We, each of us, are today better diagnosticians, better doctors, better surgeons than we were twenty years ago.

There are statistics at hand, quite as imposing and quite as reliable as those presented by my old friend, Dr. Ward, which prove that the surgical cures of early cancer of the cervix outrank those obtained with radium, even if we include the higher operative mortality. Moreover, the surgical treatment which, for a while, had been pushed into the background, has again become a very actual question. We are just now beginning to reap the harvest of the untiring educational campaign which has been sponsored in this country by the American Society for the Control of Cancer. As a result, cancer is recognized at earlier stages. Whereas ten years ago, we saw in our Barnard Free Skin and Cancer Hospital hardly one case of early cervical cancer a year, we now discover a dozen or more, and the indications for further improvement of conditions are propitious. Let no one think that the enormous benefits which we have derived from radiotherapy can be belittled. Quite to the contrary, but it should be a source of satisfaction to know that we have two modes of procedure at our disposal when attacking an early case of cancer of the cervix.

Dr. Ward (closing).—I wish to make clear to Dr. Taussig that seventeen years ago, when we first began to use radium, we were feeling our way and that in our earlier cases many were over-radiated by repeated irradiations of what had become radioresistant tissues. As our experience grew, our technic has been modified, and we use repeated irradiations only when a metastatic nodule develops in the vaginal tract, which we are able to discover early due to our method of a personal monthly follow-up inspection during the first three years.

We have without question saved many cases by this early discovery of a recurrence in a new site and re-radiation. Regaud in Paris and Heyman in Stockholm do likewise. I might ask what else can we do?

In this survey of our complications all occurring in the entire period are included. For screening we use the equivalent of one millimeter of platinum.

I am in entire accord with Dr. Gellhorn that irradiation is not the only method of value in carcinoma of the cervix, particulary in the early cases. Because there is a price to pay for radium therapy which must be considered and should be compared to that paid for radical surgery, I have written this paper.

INDUCTION OF LABOR BY ARTIFICIAL RUPTURE OF THE MEMBRANES WITHOUT QUININE*

A COMPARISON WITH SEVERAL METHODS

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Induction of labor, either premature or at term, is often a tedious if not a dangerous procedure, notwithstanding the element of uncertainty attendant upon most methods commonly used. In recent years, the work of Slemmons,[1] Guttmacher and Douglas,[2] and others has stimulated interest in inducing labor by artificial rupture of the membranes, preceded by castor oil, enema, quinine, and in some cases pituitrin administered either intranasally or hypodermically. These methods have served to increase the percentage of success, shorten the waiting period, and have given a degree of safety and certainty not felt with the older medical and surgical methods. However, Gellhorn,[3] King,[4] and others have observed and recorded fetal deaths apparently due to quinine used in the induction. Torland[5] reported a case in which 10 grains of quinine caused immediate death of the fetus, with moderately severe anaphylaxis in the mother; while Taylor[6] cites two cases in which deafness in the babies was supposedly due to the use of quinine antenatally.

It was this thought that prompted us to try castor oil, enema and rupture of the membranes as a means of inducing labor in cases in our Charity Hospital services.† In order that we might have a basis for comparison, we have studied cases induced by bag, catheter, modified Watson, with and without artificial rupture of the membranes, and cases in which the membranes had ruptured spontaneously before the onset of labor. Unfortunately we were unable to obtain 100 cases in each series. They have been taken as they have presented themselves in the wards, most of them being near or at term. In the castor oil, enema and rupture of the membranes group, there were three cases less

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†Dr. E. L. King was in a large measure responsible for obtaining these cases. It was only through his willingness, cooperation and unselfish advice that the procedures were carried out.

than 8 months pregnant (one 7 months multipara and two 6 months primipara); 7 in the catheter series (one multipara under 7 months, 4 primipara, and 2 multipara between 7 and 8 months); 5 bag cases (2 primipara, 2 multipara less than 7 months, and one multipara 7 to 8 months; and 2 spontaneous premature rupture of the membranes (one primipara and one multipara less than 7 months) less than 8 months; while all the modified Watsons, with and without rupture of the membranes, were at or near term.

The cases were divided among primipara and multipara, as shown in Table 1.

Technic.—The technic employed in cases induced by castor oil, enema and rupture of membranes was as follows:

6:00 a. m., castor oil, 2 ounces
8:00 a. m., copious hot soapsuds enema
8:00 a. m., rupture of membranes

Soon after the enema, the patient was removed to the delivery room and prepared as for delivery. The membranes were stripped from the internal os and ruptured with a hook. Where quinine was used, it was started at the time of the enema. In most of our cases an effort was made to allow free escape of amniotic fluid, 3 to 6 ounces or more. The patient was then allowed up and about the ward, and instructed to report the time of her first pain. In no case was an anesthetic necessary. Often the cervix would admit only one finger with considerable effort. It was usually stretched to about two fingers dilatation, and then the membranes were ruptured with little or no difficulty.

Where the membranes were not ruptured, in the modified Watson cases, 5 grains of quinine sulphate were administered every thirty minutes beginning at 8:30 a. m. until 20 grains were given. The chief difference from the original Watson is the elimination of pituitrin and cutting the quinine dosage from 10 to 5 grains.

Indication for Induction. — The inductions were performed because of toxemia, term and postmaturity in the largest number of cases. However, in the bag and catheter cases especially, a fairly large number were under eight months, the induction being done for some complication present at that time. Table 2 gives the indications in each group.

Table 2

INDICATION FOR INDUCTION

	C.O.E. R.M.	Mod. Wat. R.M.	Mod. Wat.	Bag	Catheter
Term	49	23	45	2	14
Post Mat.	18	6	22	2	8
Toxemia	22	11	26	10	25
Large baby	6	3	4	1	
Eclampsia	3				1
Small pelvis		1	1		1
Rupt. memb.			2	2	
Heart disease		1		1	
Plac. previa		1		1	
Dead baby			1		
Osteomyelitis	1				
Tuberculosis	1				
Pyelitis					1

One of the toxic cases in the castor oil, enema and ruptured membranes group was a twin pregnancy; another had a dead baby. The placenta previa in the modified Watson series with rupture of the membranes was the marginal type, while the one in the bag series was lateral.

Latent Period.—Using the term suggested by Guttmacher and Douglas,[2] the latent period for the cases in which the membranes were ruptured was taken as the interval between their rupture and the onset of labor; in the modified Watson group, from the last dose of quinine

Table 1

PRIMIPARA AND MULTIPARA IN EACH SERIES

Method	Primipara			Multipara			Total
	Wh.	Col.	Total	Wh.	Col.	Total	
Castor oil, enema, ruptured membranes	20	8	28	36	36	72	100
Castor oil, enema, quinine, ruptured membranes	3	1	4	28	13	42	46
Premature ruptured membranes	4	8	12	15	23	38	50
Modified Watson	17	14	31	44	25	59	100
Catheter	14	11	25	12	13	25	50
Bag	3	5	8	2	9	11	19

until the beginning of pains (two hours later than where the membranes were ruptured); and in the bag and catheter group, from their insertion until contractions started. Table 3 shows the interval in hours, with the number of primipara and multipara, and the percentage for each interval for the cases in all the series.

Table 3
THE LATENT PERIOD

Method	2 Hrs. or Less No.	Per Ct.	2-10 Hrs. No.	Per Ct.	Over 10 Hrs. No.	Per Ct.
Castor oil E.R.M. 100 cases	P. 15 M. 45	60	P. 10 M. 21	31	P. 3 M. 6	9
Catheter 50 cases	P. 4 M. 5	18	P. 11 M. 15	52	P. 10 M. 5	30
Mod.Wat. 100 cases	P. 16 M. 28	44	P. 9 M. 29	38	P. 6 M. 12	18
Wat.R.M. Mod. 46 cases	P. 3 M. 32	75+	P. 1 M. 9	21.7	P. 0 M. 1	3.3
Bag 19 cases	P. 2 M. 4	31.5	P. 3 M. 5	42.1	P. 3 M. 2	26
Pre.R.M. 50 cases	P. 5 M. 12	34	P. 3 M. 9	24	P. 4 M. 17	42

There was one primipara in the castor oil, enema and ruptured membranes group, with a 53½ hour waiting period, and several others lasted over 24 hours, while 5 cases went into labor with the puncture of the water bag. The high percentage of the modified Watson with rupture of membranes beginning labor in two hours or less may be partially explained by the preponderance of multipara, yet the average latent period is longer for multipara than primipara, as is seen in Table 4. In a primipara in whom labor was induced by catheter, pains did not start for three days. Ordinarily the catheters are removed after 48 hours; however, the vaginal pack was replaced every day.

Table 4 gives the shortest and longest latent period for cases as a whole, and the average latent period for multipara and primipara in all the cases reported.

Unquestionably the shortest average latent period is found in cases where the membranes are ruptured artificially to initiate contractions, the pre-rupture medication being in favor of quinine, but its advantage is not so great, especially for multipara, and also primipara, if the case with the 53½ hour period is eliminated from the series. The figures where quinine was used compare with 2.5 and 4.2 hours for primipara and multipara, respectively, reported by Guttmacher and Douglas.

Duration of the First Stage.—It was felt, perhaps, that the length of the first stage of labor would give a more accurate index as to the harm that might have been done by rupturing the membranes than the total labor, since dystocias due to unfavorable positions would be more manifest in the second stage. Approximately one-third of the cases in all the groups were completely dilated in three hours or less, except those in which the catheter was used, and approximately two-thirds at the end of six hours, excepting the catheter and bag series. Cases with quinine and rupture of the membranes dilate faster, apparently, than any other group, but perhaps the series is not large enough to be significant, and more of the cases should have been primipara. Table 5 shows the number of cases dilated at different periods for primipara and multipara, with their percentage, and the per cent of the total cases for that interval.

Table 4
INDUCTION OF LABOR: DURATION OF LATENT PERIOD

		C.O.E.R.M. Hours	Catheter Hours	Mod. Wat. Hours	Mod.Wat.R.M. Hours	Bag Hours	Pre.R.M. Hours
Longest	P.	53.5	72.0	50	5.5	33.5	58.5
	M.	43.9	14.0	72	24.0	13.0	72.0
Shortest	P.	0.0	1.0	0.5	0.25	1.0	0.0
	M.	0.0	0.5	0.0	0.00	0.5	0.0
Average	P.	5.34	18.5	6.14	1.94	12.05	12.8
	M.	3.98	5.24	8.0	2.21	3.5	17.38

The longest first stage in the castor oil, enema and rupture of the membranes group was 46 hours, which was that of a white para 7; and the shortest was 25 minutes, also a white patient having her seventh baby. Table 6 gives in hours the longest and shortest first stages for all cases, also the average duration of the first stage, as well as the average total length of labor for primipara and multipara in each series.

Operative Deliveries.—The tabulation (Table 7) shows the operative deliveries occurring in the cases reported in this paper. Those induced by artificial rupture of the membranes have been

Table 5

DURATION FIRST STAGE OF LABOR

		3 Hours or Less		3-6 Hours		6-12 Hours		12-18 Hours		Over 18 Hrs.	
		P.	M.	P.	M.	P.	M.	P.	M.	P.	M.
C.O.E.R.M.	No.	2	27	10	16	10	17	2	6	4	7
100 cases	Per Ct.	7.1	37.5	36	22.2	36	23	7.1	8.5	14.3	9.7
P. 28											
M. 72	Per Ct. Av.	29		26		27		8		11	
Catheter	No.	1	4	4	11	7	3	5	2	5	4
50 cases	Per Ct.	4	16	16	44	28	12	20	8	20	16
P. 25											
M. 25	Per Ct. Av.	10		30		20		14		18	
Mod. Wat.	No.	1	26	9	20	17	15	2	4	2	1
100 cases	Per Ct.	3.2	37.7	29	29	54.8	21.7	6.4	5.7	6.4	1.4
P. 31											
M. 69	Per Ct. Av.	27		29		32		6		3	
C.O.E.Q.R.M.	No.	1	16	1	13	1	9	0	1	1	1
46 cases	Per Ct.	25	37.1	25	31	25	21.4		2.4	25	2.4
P. 4											
M. 42	Per Ct. Av.	36		30.4		21.7		2.2		4.3	
Bag	No.	2	3	0	2	2	3	2	1	2	0
19 cases	Per Ct.	25	27.5		18.1	25	27.1	25	9	25	
P. 8											
M. 11	Per Ct. Av.	26.3		10.5		26.3		15.8		10.5	
Premat.R.M.	No.	1	12	4	13	3	6	2	5	1	2
50 cases	Per Ct.	8.3	31.6	33.4	34.2	25	15.8	16.7	13.2	8.3	5.3
P. 12											
M. 38	Per Ct. Av.	26		34		18		14		6	

*Not stated: catheter, 8 per cent; C.O.E.Q.R.M., 4.3 per cent; and bag, 10.5 per cent.

combined, there being only two operative cases in the quinine and rupture of membranes group.

There were only two sets of twins. One was that of a white multipara (para 6) whose membranes ruptured spontaneously 50 hours or more before the onset of labor. Her labor was finally terminated by low forceps on the first baby and a version and extraction on the second. The second twin case was a primipara in which labor was induced with castor oil, enema and rupture of the membranes. The uterus was extremely large, labor was induced promptly, and after 24 hours dilatation was practically complete, but the patient was exhausted. Dilatation was accomplished by Dührssen's incisions, and the first baby was delivered by mid forceps, the second by version and extraction. All four babies were living.

All of the low forceps were prophylactic save one, which was done on a dead baby in the in-

Table 6

AVERAGE FIRST STAGE AND TOTAL LABOR

Series	Longest	Shortest	Average First Stage		Average Total Labor	
			P.	M.	P.	M.
C.O.E.R.M.	46.0	0.42	9.06	7.73	10.18	8.50
Mod.Wat.RM.	36.5	0.42	8.39	5.39	10.17	6.17
Premat.R.M.	48.0	0.50	8.56	8.01	9.06	8.45
Mod.Wat.	24.5	0.67	8.57	5.51	9.68	6.1
Catheter	58.0	1.67	12.29	9.14	13.9	10.36
Bag	29.0	2.00	14.04	5.66	14.67	6.21

Table 7

INDUCTION OF LABOR: OPERATIVE DELIVERIES

Procedure	Art.R.M.	Premat. R.M.	Catheter	Bag	Mod. Wat.
Low forceps	4	2 (1 twin)	3	2	4
Mid forceps	2 (1 twin)	1			
Occ. Posterior	2				
Vers. and Ext.	2 (1 twin)	1 (twin)		1	
Breech ext.	1	1		1	
Percentage	8—	8	6+	24	4

terest of the mother, because of a marked toxemia. The second mid forceps (first already described in second twin case above) was done because of a prolapsed cord when the membranes were ruptured artificially in an effort to induce labor, the baby being stillborn. The third case occurred in the spontaneous premature rupture of the membranes group because of intrapartal fever, terminating with a live baby. Both the occiput posteriors were delivered by the modified Scanzoni maneuver, one following an external version, and both babies were living. Two of the breech extractions (one in castor oil, enema and rupture of the membranes series and one in the catheter group) were on six months premature babies, who died soon after birth. The breech extraction occurring in the bag cases, following a sacral left anterior position, terminated with a live child. Of the two remaining versions (two already described in twin cases) one was in the castor oil, enema and rupture of the membranes group following a prolapsed cord which occurred when the membranes were ruptured, and ended with a dead baby; while the other was the case of a lateral placenta previa where a bag had been used, this ending with a living child.

The percentage of operative deliveries is low because of the size of the services at the Charity Hospital, labors having been terminated by instruments only when a bona fide indication arose. This compares with the 16.5 per cent of cases induced by artificial rupture of the membranes reported by Guttmacher and Douglas[2] and the 19 per cent in the 14,396 full-term spontaneous labors in patients at the Johns Hopkins Clinic.

Table 8

INDUCTION OF LABOR: MATERNAL MORBIDITY

	21 Cases C.O.E.R.M.		7 Cases Mod. Wat.R.M.		12 Cases Mod.Wat.		12 Cases Premat.R.M.		18 Cases Catheter		5 Cases Bag	
	P.	M.	P.	M.	P.	M.	P.	M.	P.	M.	P.	M.
Pyelitis	5	4		2		1		1	1		1	
Breast		2										
Bronchitis	1							1				
Before ind.	1											
Long labor		1										
Breech ext.		1										
Pyelocystitis before ind.										1		
Sepsis					1		1	1	1	1	1	
Not explained	4	2	4	1	5	5	2	6	5	9	1	2
Percentage not explained	6		9+		11		20		32		21	

Morbidity.—Cases have been considered morbid where the temperature reached 100.4° for longer than one day, or had risen above this height for one day or more.

This gives a morbidity of 6 per cent for the castor oil, enema and ruptured membranes group, as compared with 9+ per cent for the castor oil, enema, quinine and ruptured membranes group, and 20 per cent where the membranes ruptured prematurely. It is clear from the table that febrile cases were more numerous with the bag and catheter, and that sepsis is much more likely to occur following intra-uterine manipulation, and also where the membranes have ruptured long before the onset of labor. The one septic case, a colored multipara, in the spontaneous premature rupture of membranes, had a 48-hour latent period, while the case with a latent period of 53½ hours was afebrile. The table below (Table 9) gives the latent period in each febrile case where the membranes were ruptured artificially, the upper group having had no quinine.

Table 9

INDUCTION OF LABOR: FEBRILE CASES IN ARTIFICIAL RUPTURE

Case	Para	Latent Period	Day's Fever	Duration Labor
1	C VI	2½ hrs.	101—1 day	4¾ hrs.
2	W I	1½ hrs.	101—3 days	2 hrs.
3	W II	1 hr.	101½—1 day	8 hrs. 27 min.
4	W II	6 hrs.	101—1 day	47 hrs.
5	C I	36 hrs.	103—1 day	5 hrs. 35 min.
6	C I	2 hrs. 10 min.	101—2 days	8½ hrs.
1	C VII	2 hrs.	101-102—4 days	4 hrs. 10 min.
2	W III	4 hrs. 45 min.	101-103—4 days	5 hrs. 15 min.
3	W I	15 min.	100 102—4 days	23 hrs. 45 min.
4	C IV	1 hr. 25 min.	103—3 days	9 hrs. 45 min.
5	C III	1 hr.	101—1 day	Short

It is apparent that the temperature in none of these cases was high and that they were not septic cases. Case 6 in the first group and Case 2 in the second group may be explained by the forceps and prolapsed cord in the first instance and the placenta previa in the second. However, the rates here of 6 per cent and 9 per cent, respectively, compare with the 7.6 per cent (Wilson) and 10.8 per cent (Guttmacher and Douglas).

Fetal and Maternal Mortality.—In the entire series there were 24 babies who died soon after birth or were stillborn. The tabulation (Table 10) shows how they were distributed as to cause in each group.

Table 10

INDUCTION OF LABOR: FETAL MORTALITY

	C.O.E.R.M.	Catheter	Bag	Mod.Wat.	Spon.R.M.	Mod.Wat.R.M.
Premature	2	3	4		1	No
Macerated	1	1	1	1	1	fetal
Toxemia		2*				deaths
Long labor			1*			
Prolapsed cord	2*					
Atelectasis	1					
Not explained			2*			
Total	6	6	8	1	2	
Corrected mortality per cent	2	4	15	0	0	0

*Fetal deaths due to induction.

The two cases of prolapsed cord were in term primipara, both colored. One was a case of polyhydramnion, and the other was one in which the patient was not allowed up after the membranes were ruptured; however, the cord prolapsed late in the first stage. Both the toxic babies in the catheter group were full term, the mothers being only mildly toxic (not sufficient to explain the fetal death). While the one case in the bag series with a long labor was probably not due to the induction, yet it is only fair to charge this death to that method. The modified Watson group had only one fetal death, that of a macerated fetus, labor being induced because of this. This is somewhat contrary to the motivating thought of this paper; however, most of these cases were uncomplicated and at term. Crowther-Smith,[7] reporting the results at Guy's Hospital, where a method similar to this was used in 128 successful trials, recorded six fetal deaths due to asphyxia alone.

The corrected fetal mortality for all cases in which the membranes were ruptured artificially in this series is 1.37 per cent, which corresponds favorably with 3.49 per cent reported by Rucker,[8] 3.5 per cent of Stern,[9] about 4 per cent by Wilson,[10] whose one death in 26 cases was a prolapsed cord occurring soon after the membranes were ruptured and 5.16 per cent in the past 14,396 normal, spontaneous labors at Johns Hopkins Clinic.[2] There were no maternal deaths in any of the series.

Attempts at Induction.—To date no method of inducing labor is satisfactory and dependable in every respect. However, one nearest to fulfilling this requirement would initiate labor promptly, would not hinder progress or affect the mother or fetus deleteriously, and could be depended on at all times. The modified Watson method is probably the most extensively used, and is about the least dependable. Yet, cases started with it usually go on to a successful end. Rupture of the membranes with any method increases the efficiency of that method. The modified Watson was tried one or more times on some of the cases in all groups. Table 11 shows the number of unsuccessful attempts in each series.

Table 11

INDUCTION OF LABOR: UNSUCCESSFUL ATTEMPTS

Induced by ↕	Mod.Wat.	Catheter	Watson	Pituitrin
C.O.E.R.M.	19	1	1	3
Mod.Wat.R.M.	13			
Mod.Watson	27			
Catheter	34		3	
Bag	6			1
Total trials	99	1	4	4

In 199 attempts at induction with the modified Watson technic there were 100 successes, or a percentage of 50.2. This is about the percentage given by McGoogan[11] in 29 successful cases.

All cases in which the membranes were ruptured artificially went into labor. One case, however, had a latent period of 53½ hours, and for some reason did not get pituitrin. In no case was it necessary to use the bag, but pituitrin was given because of slowness of starting in two cases of the castor oil, enema, rupture of membranes group, and one that had quinine and ruptured membranes was also packed because of marked maternal toxemia.

DISCUSSION

Castor oil and quinine have been used separately and jointly as a means of inducing labor for years. Yet, a review of some of the pharmacologic texts on the action of castor oil fails to mention any oxytoxic property of this drug. Scott[12] says:

> "Ricinoleic acid enters the blood and tissues and is excreted with the various secretions of the body, imparting its purgative qualities to the milk of the mother."

It does not seem unlikely that this acid might have some mild stimulating action on the uterine musculature in pregnancy, and in this way

aid considerably in starting labor. Sollman[13] says:

"There is some pelvic congestion, so that it is to be avoided in pregnancy and menstruation."

Whatever its action, whether reflex, toxic, or due to increased pelvic blood supply, other cathartics fail to give the same results.

That quinine is toxic to certain individuals is a well established fact. Scott,[14] in summing up its reaction in some cases, says:

"Individual idiosyncrasies are frequently observed with regard to the action of quinine. In some persons even small doses produce a severe erythema and urticaria, with submucous edema, often followed by desquamation of the cuticle and accompanied by pronounced disturbance of the nervous system and circulation." He says further: "It acts as a uterine stimulant in labor and is used as an oxytoxic, but its power to initiate uterine contractions is strenuously denied by many investigators."

We have used it many times in malaria complicating pregnancy, without initiating labor.

A white primipara at term, where the modified Watson method was used, showed a slight quinine anaphylaxis in the nature of a moderately severe urticaria. Her baby, weighing seven pounds eleven ounces, was living and delivered spontaneously. This is the only case in our series where any untoward reaction to quinine was noted.

Our experience with rupture of the membranes as a method for inducing labor has been limited to vertex cases. However, Slemmons[1] has used it in breech cases with success. There are certain advantages, such as shortening the labor 40 per cent or more in both primipara and multipara, and increasing the certainty of the onset with an average latent period of 25 to 50 per cent less than is found in cases induced with the modified Watson, catheter, or bag. Although the length of labor and latent period is shorter in cases where quinine is used, we believe that probably with a little more refinement of technic and judgment in selecting cases, these will be reduced.

Prolapsed cord is a danger that can hardly be escaped when the membranes are ruptured. For this reason, the head or presenting part should not be high at the time of rupturing the membranes. This was brought out by Rucker[8] and Wilson,[10] the latter reporting a slightly premature case where the prolapse occurred immediately after the membranes were ruptured. Guttmacher and Douglas[2] had a similar experience in a polyhydramnion. We feel that in at least one of our cases this might have been prevented had the patient been allowed up following the puncture. Wilson[10] uses a special instrument to rupture the membranes, which prevents a gush of water. This is probably better than the hook method. One case, that of a colored multipara at term, in the castor oil, enema, quinine and ruptured membranes group, immediately after the membranes were ruptured, was followed by a prolapse of both hands. They were replaced and the patient went on to a normal spontaneous delivery with a live baby.

No effort was made to study the relationship of the latent period and the length of labor to the degree of dilatation and effacement of the cervix. However, in no case were the membranes ruptured where the cervix was longer than three-quarters of an inch, regardless of dilatation. Jackson, discussing his results in 500 cases, said:

"If the cervix is not flattened with a long canal and an unopened os, labor will be induced by rupture of the membranes, but the total labor will be longer and the latent period definitely increased." However, he believes that "rupture of the membranes is essential for a sure start of labor," and says further, "if the cervix is flat or thin when the membranes are ruptured, the start of labor is usually instituted so quickly and with such satisfaction that pituitrin is not necessary."

It is interesting to note that Crowther-Smith,[7] in comparing the methods used at Guy's Hospital, decided that rupture of the membranes was unphysiologic and should never be used.

Wilson[10] had two rather hazardous experiences in his series. One was a colored hypertensive heart case with dyspnea and cyanosis for three days before induction. She died fifteen minutes after the membranes were ruptured. The other, with mitral stenosis, almost died following rupture of the membranes. She became cyanotic and frothed at the mouth, but at the end of an hour was comfortable and delivered spontaneously. Rucker[8] encountered a large number of contraction rings in his cases. This has not been our experience, but it should be borne in mind as a possible complication. Three eclamptics in which castor oil, enema and rupture of the membranes was used, in our series, to induce labor, all terminated spontaneously; one with a 20-minute labor (para IX), and the other two after five hours and 30 minutes (para I and IX), the three with live babies.

An advantage, as pointed out by Stern,[9] is the elimination of the element of uncertainty as to the date of the confinement. This is an ad-

vantage especially in nervous, excitable women, and in cases with contracted pelves, where a few days might mean the difference between a vaginal delivery and an abdominal section. On the other hand, Stern recommends it for all cases as a routine method of controlling the birth date as well as the hour for delivery. This seems somewhat radical and one who practices it routinely is likely to meet with difficulty.

SUMMARY

There is little doubt that induction of labor by artificial rupture of the membranes, preceded by some suitable pre-rupture medication, shortens the latent period, first stage, and total labor. It must be borne in mind that all cases do not readily lend themselves to this method. Where the cervix is long and the canal tightly closed, catheter induction is to be preferred, maintaining the membranes intact, because they are undoubtedly a valuable aid in the thinning out process. Cases in which there is some dilatation, with the membranes already ruptured, are probably better completed by the use of a bag. Most of the bag cases in this series were considered difficult and in evaluating its merits the length of the latent period and total labor would probably have been as long by any method where the membranes are ruptured artificially, as the average of these shown for the bag cases. However, we feel that there is a definite place, in selected cases, for the induction of labor by artificially rupturing the water bag.

Although the series reported in this paper where labor was induced by castor oil, enema and rupture of the membranes is too small to draw any definite conclusions, there are some points that should be emphasized:

(1) Artificial rupture of the membranes is a method of advantage in inducing labor in selected cases. The absence of quinine in the induction is not a serious drawback, and in many cases it is an advantage, where idiosyncrasies to quinine are present, since it may save babies and mothers who might otherwise be lost.

(2) Quinine is toxic to certain individuals, and has been ascribed as the cause of fetal deaths, and possibly deafness in the child. For these reasons its use is not entirely safe in all cases, since those in whom untoward reactions are likely to occur cannot be predetermined.

(3) Spontaneous premature rupture of the membranes is followed ultimately by onset of pains. However, the onset may be delayed as long as two to three weeks, which apparently is not the case where some suitable pre-rupture preparation is used.

(4) Intra-uterine manipulation with bags or catheter predisposes to sepsis and high maternal morbidity, which is obviated in cases induced by artificial rupture of the membranes.

(5) Rupturing the membranes carries with it an element of fetal danger, namely, prolapsed cord and compound presentations. The first is likely to occur in any case of polyhydramnion, whatever the method of induction, and also in cases where the presenting part is high. We believe that this complication is no more likely to occur in cases where quinine has been omitted, although both of ours were in that group, since Wilson and Guttmacher and Douglas reported a case in their series where quinine had been used. Selecting cases with the presenting part fairly well down, though not necessarily engaged, allowing the patient on her feet following the rupture, along with the use of a suitable instrument, which will permit the amniotic fluid to be released slowly instead of with a gush, will probably completely eliminate this complication.

(6) Apparently artificial rupture is contraindicated in heart disease, in that a sudden escape of fluid may be the cause of a cardiac collapse and death.

(7) Castor oil plays an important role in the induction of labor. Just what its action is, is not clear. Suffice it to say that other cathartics fail to produce the same effect.

BIBLIOGRAPHY

1. Slemmons, J. Morris: The Induction of Labor at Term. Amer. Jour. Obst. & Gyn., **23**:494-501 (April) 1932.
2. Guttmacher, Alan F.; and Douglas, R. Gordon: Induction of Labor by Artificial Rupture of the Membranes. Amer. Jour. Obst. & Gyn., **21**:485-497 (April) 1931.
3. Gellhorn, George: Can Quinine Kill the Fetus in Utero? Amer. Jour. Obst. & Gyn., **13**:779 (June) 1927.
4. King, E. L.: Does Quinine in the Induction of Labor Have a Deleterious Effect on the Fetus? J.A.M.A., **101**:1145-1148 (Oct.) 1933.
5. Torland, Torleif: Fetal Mortality After Induction of Labor by Castor Oil and Quinine. J.A.M.A., **90**:1130 (April 14) 1928.
6. Taylor, H. Marshall: Pre-Natal Medication as a Possible Etiologic Factor in Deafness in the New Born. Arch. Otolaryng., **20**:790-803 (Dec.) 1934.
7. Crowther-Smith, Edward Hughes de Barros: Guy's Hospital Report, **84**:250-256 (April) 1934.
8. Rucker, M. Pierce: Artificial Rupture of the Membranes as a Means of Inducing Labor. West Va. Med. Jour., **31**: 54-56 (Feb.) 1935.
9. Stern, Samuel M.: Routine Induction of Labor at Term. Amer. Jour. Obst. & Gyn., **27**:701-704 (May) 1934.
10. Wilson, L.: Induction of Labor by Rupture of the Membranes. Amer. Jour. Obst. & Gyn., **27**:265-269 (Feb.) 1934.
11. McGoogan, Leo S.: Induction of Labor. Neb. State Med. Jour., **20**:67-71 (Feb.) 1935.
12. Scott, A. J. S.: Potter's Therapeutics, Materia Medica, and Pharmacy, 15th Edition, p. 434. Philadelphia: P. Blakiston's Son & Co., Inc., 1931.

13. Sollman, Torald: A Manual of Pharmacology, 3rd Edition, p. 231. Philadelphia: W. B. Saunders Company, 1927.
14. Scott, R. J. S.: Potter's Therapeutics, Materia Medica, and Pharmacy, p. 295. Philadelphia: P. Blakiston's Son & Co., Inc., 1931
15. Jackson, Delbert L.: Rupturing Membranes to Induce Labor. Amer. Jour. Obst. & Gyn., **27**:329-336 (March) 1934.

DISCUSSION (*Abstract*)

Dr. Wm. T. McConnell, Louisville, Ky.—The chief factors of value in any procedure of induction of labor are, first and foremost, safety; and second, reliability. From earlier work the matter of relative dependability of the methods under discussion has been very well determined, but only after consideration of many reports and many individual cases can definite conclusions be drawn as to their relative safety.

From our information at present, rupture of the membranes and bag insertion are the methods most certain to induce labor. In these two procedures the patient is rendered unfit to a varying degree for cesarean section, especially so in bag induction. In border line cases where laparotomy may have to be done it would be better to confine our efforts to medicinal inductions.

In regard to the various drugs used, probably the least valuable is quinine. Apart from the untoward effects such as allergy, deafness produced in the fetus and sometimes fatal complications, in our experience the drug is not so effective as castor oil. Before quinine is given great care should be taken to ascertain any hypersensitivity. Untoward effects from castor oil are negligible. For practical purposes the drug can be used without fear of any distressing after effects, and in our personal experience it has seemed to work as well alone as when quinine and castor oil were used together.

Small doses of pituitrin before labor sets in have not a great deal of ill effect upon the uterus. There is observed, however, an occasional tonic uterine contraction with aphyxia of the fetus. Allergic reaction is probably not so infrequent as was formerly supposed. We have encountered five clearly defined and thoroughly proven cases in our City Hospital Clinic within the past year. Probably the best method of administration of pituitrin is in the nasal pack which can be removed immediately upon the appearance of untoward effects. Neither pituitrin nor quinine should be used in hypertension cases. Castor oil, however, is perfectly safe. In the mechanical methods of induction, premature rupture of the membranes is not ideal in cases of marked prematurity. Preservation of the amniotic sac protects the premature fetus from some of the birth trauma. Bag induction is probably preferable in these cases. Mature babies stand rupture of the membranes very well, indeed. In fact, recent statistics seem to indicate that there is no demonstrable harm to the baby nor the soft parts of the mother and that labors are thereby shortenend.

Dr. E. Lee Dorsett, St. Louis, Mo.—While there is always danger in any form of induction of labor, probably rupture of the membranes has the least danger. If this method is followed care should be taken that there is not a breech presentation present or if a vertex presentation that the head is not engaged. Induction by means of a bougie is dangerous because it may loosen the placenta. Bag induction, while used by a great number of obstetricians, may result in prolapse of the cord and there is no question that it produces a labor that is longer than normal and certainly much more painful. Personally I do not fear the use of quinine and this is supported in Gwathmey's method of "painless childbirth."

Dr. Walter W. Wells, Oklahoma City, Okla.—Dr. Reddoch has outlined a good treatment and he seems to have had good results with it, but it seems to me that it would be better to try non-operative methods first. We do not care to make vaginal examinations or any vaginal or interuterine manipulation if it can possibly be avoided because of the danger of infection. I have had good results from castor oil alone: two ounces given at midnight and in the morning a hot soap suds enema. I believe the uterus is stimulated to contraction by the intestinal peristalsis through the pelvic and uterine plexus.

Because of the slow action of castor oil we should not expect early results. When I use castor oil and quinine I give two ounces at midnight and in the morning five grains of quinine; one hour later a hot soap suds enema; one hour later five grains of quinine. Repeat the quinine until the patient is in labor or twenty-five grains of quinine have been given. If she is not in labor one hour after the last dose I give another hot soap suds enema. I believe we should try out the castor oil and hot soap suds enema and if we obtain no results within twenty-four hours then try the treatment outlined by Dr. Reddoch.

Dr. Reddoch (*closing*).—I realize this is not a complete report; on the other hand, we believe that there is an advantage in omitting quinine from the induction procedure when the membranes are ruptured. We hope to have more cases ourselves in the near future, and also that others will try it.

INTRACELLULAR PARASITISM AND THE CYTOTROPISM OF VIRUSES*

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The study of animals in their relation of host to parasites has shown that the healthy animal body possesses a very great resistance to infection by all but a relatively few species of microorganisms. Nevertheless, examples of pathogenic microbes may be found in widely separated groups of living agents, notably among the bacteria, fungi, spirochetes and protozoa. Of recent years still another group of pathogenic agents has received much attention, namely, the viruses, which are at present in a class by themselves suspended in judgment of their nature between the living and the inanimate.

From certain aspects it appears perhaps for-

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tunate that viruses resist isolation by culture, for when it becomes easily possible to cultivate the causative agent of a particular disease in pure strain on a dead medium there is a tendency for the pathologist and the parasitologist to separate, the one to lose somewhat of interest and curiosity in pathogenesis, the other to become too much absorbed with the non-parasitic existence of the micro-organism concerned.

Koch,[1] before he had invented solid media for the isolation of pure cultures, stated that "there exists no better cultivation apparatus for pathogenic bacteria than the animal body itself." Certain it is that when pathogenic micro-organisms are studied apart from the lesions they induce, and lesions are studied without particular emphasis upon the relation of the parasite thereto, much of importance in the pathogenesis of infection will be lost.

At the present stage of virus research the investigator can study the infective agent only in connection with the lesions of the host, and he therefore becomes acutely confronted with problems of invasion, the relation of the infectious agent to the lesion and other matters of pathogenesis which demand a formulation of questions concerning the host-parasite relationship which knowledge of bacteriology and parasitology in general does not answer.

One of the pressing problems of virus research is the relation of a given virus to the cells of the host which it specifically affects. Does a virus regenerate itself outside, upon or within the cells? If one should be able to answer this question by observation or experiment, of what import would it be with reference to an understanding of the infective process?

An exact apprehension of the host-parasite relationship from the time of invasion to the end of the state of parasitism is not only a matter of great theoretical interest, but such knowledge would direct any scientific prophylactic, therapeutic and immunizing program undertaken for practical purposes.

In considering the relationship of viruses to the cells of the host it is instructive to refer to what experience of long study has taught concerning the host-parasite complex in better understood infections in which the invading agent has been cultivated or recognized morphologically.

It seems to be generally recognized since Koch's studies of anthrax, even though often not specifically stated, that many pathogenic bacteria, after entering the body fluids, grow in this medium at least during the early stages of infection. Reproduction in blood plasma is implied by Koch in his study of mouse septicemia, but he specifically stated that the bacillus of this disease grows readily and rapidly within circulating leukocytes which finally rupture. Thus in these early studies when the "best cultivation apparatus" for pathogenic bacteria was the animal body itself, two essentially distinct mediums of the host were recognized as suitable for *in vivo* bacterial growth, namely, the body fluid and the cells.

All of the early students of infectious diseases must have observed on occasion the presence of the infecting parasites within the bodies of cells, but the inherent principle of phagocytosis as a mechanism of defense against parasitic invasion was not duly recognized until Metchnikoff[2] had made his brilliant studies of this phenomenon. So impressive were his discoveries and so cogent his reasoning that many of his followers have doubtless gone further than he himself would have advocated in considering the mere occurrence of parasites within cells as *prima facie* evidence of a combative response of the invaded host, the tendency of which is toward the localization and disposal of the invader.

The serologists and immunologists were not slow to recognize that normal blood fluid is, generally speaking, not only unfavorable but actually antagonistic to bacterial growth. Under these circumstances one feels justified in accepting the general proposition that under healthful conditions both the cells of the body to which bacteria may gain entrance and the circulating blood plasma are antagonistic to most pathogenic types which are cultivable on dead media.

Pathologists and bacteriologists speak usually in general terms when referring to the invasion of the tissues of the host, failing to specify exactly what the initial conditions of invasion are. It is, I think, quite commonly accepted that in most bacterial infections due to cultivable parasites, the disease-producing agents are found to be located extracellularly, that is, in the body fluid in progressive stages of infection. Their presence within phagocytes is ordinarily regarded as a manifestation of resistance to, rather than a facilitation of, an advance in the infective process. That this is not always true has been suggested by J. A. Arkwright[3] in the following paragraph:

"True virulence or invasive power perhaps means that the invading microbe is so constituted that the first

reaction of the host is favorable to its infecting progress, and this may be the chief difference between a virulent and a non-virulent organism. Effusions of liquid which are unable to kill often appear to an unprejudiced observer actually to help the bacteria. Even leukocytes may not be disadvantageous if they take up but cannot kill and digest the microbes. They may then help them to spread by transporting them to other parts of the body. They may even form suitable sites for the multiplication of the bacteria, as appears to happen in gonorrhea and cerebrospinal meningitis when the polymorphonuclear leukocytes certainly do not soon kill all the bacteria they engulf."

It is to be added that bacteria may also be protected from some injurious influences in the environment by incorporation within leukocytes, as was proven several years ago by Rous and Jones.[4]

But the type of fluid medium is variable. For example, the cholera vibrio grows within the alkaline intestinal juices, the diphtheria bacillus on a surface bathed with a serofibrinous exudate, while the pyogenic cocci lie in or upon partially dissolved necrotic tissue, in serous exudate or in frank pus. So the optimal conditions of infection, though extracellular, seem to be different for each bacterial type, and the exact requirements for each are apparently incompletely understood. To the fluid medium fixed and mobile cells no doubt contribute elements which may determine its availability for bacterial growth.

Let it be emphasized at this point that those pathogenic agents, whether bacterial or protozoan, which are found during the active infective period to grow in an extracellular position, are precisely the ones which the bacteriologist and protozoologist have been able to cultivate most readily upon dead media in the test-tube, and it is upon this group of cultivable microbes that the most active research into the nature of infection and parasitism has been pursued; and largely upon the results of such studies have been erected our most current concepts of the host-parasite relationship, and of immunity.

It is not a valid conclusion, however, that the presence of micro-organisms within cells is always indicative of a defensive reaction of the host to invasion by the parasite. May it not sometimes be that optimal conditions for parasitic growth are to be found within a specific intracellular medium?

In attempting to answer this question it is necessary to consider some of the instances and circumstances of intracellular localization of parasites in general and to deduce from a variety of phenomena the significance which may be justifiably drawn from them.

It is well known that there are cells generally distributed throughout the animal body which constitute a tissue, partly mobile, partly fixed, which is especially concerned in the processes of phagocytosis. This tissue briefly consists of circulating leukocytes, both mono- and polynuclear, wandering cells of the tissues, serosal cells and the fixed and semi-fixed reticulo-endothelial system.[5] That this tissue or some of its elements is actively concerned in the removal, isolation and destruction of the invading germs of many infectious diseases through the process of phagocytosis, there can be no reasonable doubt. But there exist infectious diseases in which the invasive parasites are to be found within cells of this tissue in great numbers, apparently suffering no injury as a consequence of their intracellular position, and in a variety of ways lending evidence for the conclusion that they are vegetating in a congenial environment. Instances of this kind are to be found not only in bacterial infections, but in those due to fungi and protozoa as well. For example, I would place within this group the presumptive bacterial diseases human and rat leprosy, para-tuberculosis of cattle, granuloma inguinale and rhinoscleroma, the fungus infections histoplasmosis of Darling and farciminosus, and the protozoal disease, kala-azar. In addition to these there belong to the same general group the small parasites classified as Rickettsia, which likewise inhabit cells of the phagocytic system in such diseases as typhus and Rocky Mountain spotted fever.

There are certain appearances and circumstances in these cited instances of acceptably infectious diseases which entitle them to separate consideration from the numerous infections in which the role of the phagocytic tissue may be judged to be essentially defensive in its reaction. In the first place the intracellularly situated parasites do not apppear to be at a disadvantage as a result of their intracellular environment. They do not show as a prominent or characteristic feature evidences of degeneration. Rather do they appear to be in a wholesome state and generally in such numbers as to preclude or at least to bring into question the possibility that phagocytosis can account completely for their incorporate relationship. The fixed character of the leprous cell and their enormous content of acid-fast bacilli dispersed and in globi speak rather for intracellular growth. The tissue cultural experiments of Pinkerton and Hass[6] are to be explained rationally only on the basis of intracellular reproduction of the Rickettsia of typhus and Rocky Mountain spotted

fever. Histolgical and cultural investigations of DeMonbreun[7] and others on histoplasmosis and farciminosus justify a similar conclusion with reference to these fungus infections, and in kala-azar the protozoan parasites of Leishmann and Donovan are in a phase of development which is not known to multiply as such outside the medium of these living cells.

In progressive stages of each of these diseases it is the living cell of the phagocytic tissue which appears to play the passive role in the host-parasite struggle for dominance, serving merely as a nourishing and protecting medium, probably increasing its metabolic activity only to lend additional and renewed support to its parasitic burden.

In considering this group of infectious diseases in which the cell-parasite relationship concerns the normally phagocytic tissue of the animal body, it is advisable to examine the evidence of intracellular growth perhaps more critically than would be necessary in the case of a similar cell-parasite relationship in which the type of cell concerned should be of a different order, and under usual conditions at least non-phagocytic, such as the various epithelia. For example, when the bacillus of leprosy is found in masses and globi within the epithelial cells of renal tubules, Tyzzer's bacterium of a disease of Japanese waltzing mice in the epithelium of the intestinal tract and liver,[8] the bacillary organism of Wright and Craighead within ganglion cells of the central nervous system and renal epithelium in the rabbit,[9] *B. tularense* in parenchymal cells of the guinea pig's liver[10] and *B. abortus* in chorionic epithelium of the embryonic calf,[11] one feels little hesitation in assuming an intracellular growth of these bacterial forms.

Protozoology, however, furnishes more numerous and more graphic illustrations of intracellular parasitic growth than does bacteriology, for the more complex forms of these animal parasites furnish indisputable evidence of stages of intracellular multiplication. One need only refer to the cyclic development of coccidia in intestinal and biliary epithelium.

Here again it is to be observed that the protozoologist has not yet succeeded in cultivating on dead media any of those protozoal forms which are only found in vegetative phases within the living cells of the host.

In addition to the group of parasites which grow in the body fluids and those which seem to require an intracellular environment, there are at least a few bacteria which have a peculiar reproductive relationship to the surface of certain cells, namely, *B. pertussis* and *B. bronchisepticus*. Study of the ciliated epithelium of the respiratory tract in whooping cough has led me to think that *B. pertussis* reproduces itself to its greatest extent, if not entirely, in intimate relation to the ciliated border of respiratory epithelium. Evidences of growth stop sharply in the lungs where the ciliated and squamous epithelium meet. It is to be observed that these cellular surface bacteria, like those of the body fluids, have been cultivated on dead media.

This brief reference to specific instances of bacterial, rickettsial, fungous and protozoal diseases is sufficient at least to call attention to a group of infectious processes due to visible parasites in which the micro-organisms concerned seem to reproduce intracellularly in symbiosis with cells of the host. This group stands in sharp contrast to that in which the infective agent regenerates itself freely in the fluids of the host. In the first place, it is to be noted that its members resist cultivation on non-living media, while those of the latter group in which it is evident that vegetative stages of the parasites inhabit the body fluids, have been cultivated artificially in the absence of living cells.

There are of course intermediate examples between those parasites which are known to grow readily and freely in certain body fluids and are cultivable without difficulty, and the opposite extreme in which known parasites are recognized to grow within the living cell and have thus far absolutely resisted all attempts at cultivation outside. *Bacterium tularense, Bacillus abortus, Bartonella bacilliformis,* and histoplasma are instances of such intermediate parasites, for while they may be found in the host in such relationship as to justify the conclusions that they are capable of growing in cells, they have also been cultivated on dead media; it is true in most instances with some difficulty.

Sufficient evidence I believe is therefore at hand to enable one to recognize three groups of parasites divisible on the basis of their vegetative relation with living host cells, namely, extracellular parasites, facultative intracellular parasites, and obligate intracellular parasites.

If one contrasts members of the two extremes, namely, extracellular parasites and obligate intracellular parasites, with reference to the different phenomena and stages of infection and resistance, it will be seen that important theoretical and practical principles are involved which differ importantly in the two groups. It is possible in this discussion to call attention only

to a few of the contrasting phenomena and briefly to consider them.

It is evident that any portal of entry would be a satisfactory nidus for the establishment of infection by extracellular parasites provided a suitable fluid medium be established at the locus of injury. This is a variable factor, but is dependent upon conditions which influence the composition of the body fluids. Obligatory intracellular parasites must on the contrary be brought into direct contact with the type of cell which affords suitable intracellular conditions for their growth. The possibility of an intervening mechanical transportation with currents of body fluid or within the bodies of mobile phagocytes is a condition to be thought of in each instance of infection.

Invasion of the host following entry and favorable localization depends in the case of the extracellular parasite, without consideration for the moment of the intervention of defensive mechanisms, upon the extent and accessibility of favorable body-juices, but in the case of the intracellular parasites it is dependent upon the locus and accessibility of susceptible cells.

Quantitative reproduction of parasitic elements in the two cases would be determined by the amount and accessibility of favorable extracellular fluid in the case of extracellular parasites, and on the number of cells penetrated by the parasite and on hypertrophy and multiplication of invaded cells in the case of obligatory intracellular parasites.

Dissemination and elimination of the infectious agent would be influenced by the disposal by the body of infected fluid, and on the rupture and discharge of infected cells respectively in the two contrasting instances.

With respect to possible defensive mechanisms involved in the two cases there can be little doubt that they, too, would be equally contrasting. If one eliminates for the moment consideration of phagocytosis and the thereby possible intracellular destruction by the unfavorable action of the living cellular protoplasm, one may imagine the struggle of the extracellular parasites on the one hand against presumably increasing humoral antibodies which tend to inhibit growth and extension, and the contest between the intracellular parasite and its cell-host on the other hand, as the cell conceivably builds up a resistance to the invader or becomes injured thereby while the latter attempts to protect itself against an increasingly uncongenial environment. But in addition we would expect in the case of the obligate intracellular parasite another contest in its attempt to reënter cells after it has been discharged from one cell-host and becomes acted upon by an acquired antiparasitic serum, or becomes confronted by a cell which has acquired a resistance to penetrability. Should the invading parasite again become incorporated by a once susceptible cell it might find upon its entry that the formerly congenial cell-host has become super-sensitive to its presence and rapidly dies before the invader has so adjusted itself that multiplication can take place, or has become otherwise an unsuitable medium for a continuance of parasitic reproduction. Thus the infection may be ended. Again we may picture in our minds a condition in which during the course of infection sufficient antigen from the obligate cellular parasite has been absorbed to cause a humoral antibody response which is able to destroy any of the parasites which become exposed to it, but is incapable of reaching the vegetative forms which remain protected from the outside environment by their intracellular position. Thus the infection may remain latent.

The fact that bacteria harbored within the bodies of phagocytic cells themselves may be protected from the action of serum antibodies was demonstrated several years ago, and recent researches upon viruses indicate a similar protection of the infectious agent by the cell-virus relationship.[12]

Perhaps a more summary contrasting of some of the theoretical possibilities which would tend to combat or overcome infections due to extracellular parasites on the one hand and obligatory intracellular parasites on the other would bring out more clearly the distinction which I am trying to make.

From much experience in the investigation of extracellular bacterial infections immunologists have brought to light certain prominent sources of defense by the infected animal against these agents, namely, humoral antibodies, natural or acquired, phagocytosis, and a rather indefinite local tissue immunity, not easily separable from phagocytic phenomena. On the other hand, one may postulate several different hypothetical mechanisms which conceivably take part in controlling or terminating infections by an obligate intracellular parasite, in addition to the effects of fluid antibodies as a lytic mechanism or as a preparation for phagocytosis. The fluid antibodies might so act upon exposed obligate intracellular parasites that they are rendered incapable of penetrating other cells; a change might occur at the surface of cells which thereby resist

attempted reëntry of a parasite; a cell might become hypersensitive so that it would be greatly damaged or die before the reëntered parasite could multiply; a change might occur in the intracellular medium rendering it no longer suitable for parasitic growth, whereupon the entered parasite becomes latent or dies; and a change might occur in the cell-host rendering the parasite innocuous, so that its growth may continue without causing disease, unless it enter a new and susceptible host.

Briefly there are many parasites of various kinds which seem to find optimal conditions for reproduction within the protoplasm of living cells of their hosts and it appears in the case of most of those examples which have been cited that, under natural conditions, an intracellular medium is essential for their continued existence. This intimate and restricted form of parasitism differs in many important particulars from that in which the invading micro-organism multiplies and extends only in body fluids of one sort or another. The two types of parasitism involve in part at least a contrast in pathogenesis and in mechanism of host resistance.

The filterable virus group of infectious agents resemble in their general character, in so far as this is known, rather the obligate intracellular parasites; and in a few instances experimental evidence has been adduced which locates the virus within the cytoplasm of specific cells of the host.[13] However, there is as yet lacking proof of the parasitic nature of any virus and final judgment in this regard must at present remain suspended. The recent work of Stanley indicates that a mosaic disease of tobacco is due to an inanimate substance, an autocatalytic agent, which is at the same time disease-inducing and elaborated by the cell it injures.[14]

In this state of affairs it is advisable to use the term cytotropism rather than parasitism when referring to the peculiar relation of viruses to the susceptible cells of the host. However, because of the fact that viruses are known to be antigenic it would seem that the same general principles which are applicable to obligate intracellular parasites are operative under the circumstances of viral infection. For if viruses are autocatalytic ferments they are certainly derived from within the cell, unless they generate spontaneously, and if they are living micro-organisms the best evidence available indicates a similar site of pullulation.

The concept of cytotropism of viruses in relation to their hosts is at present an experimental hypothesis and should be viewed as a favorable starting point from which to construct a profitable, productive program of research. Like the fact of obligate intracellular parasitism, the implications of cytotropism are numerous and important. Many of the phenomena of infection by viruses may be explained by this hypothesis, for example, their resistance to cultivation on dead media, their specific effects upon certain cells, such as the occurrence of cytoplasmic inclusions in fowl-pox, and the extension of neurotropic viruses along nerves.

The hypothesis also would seem to be a useful one in investigating from a practical standpoint the all-important problems of resistance and immunity to virus diseases. For example, one finds recorded observations on resistance to certain virus infections which are difficult to reconcile with experience accumulated from the study of extracellular parasitic infection. Numerous investigations have disclosed an increase of susceptibility of animals, as a result of malnutrition and vitamin deficiencies, to infection by a variety of extracellular and cultivable micro-organisms, but similar conditions in the relatively few observations recorded, indicate that the reverse is true for at least certain virus infections. Thus it has been observed that guinea pigs not gaining in weight and in poor general condition do not react well to the virus of foot-and-mouth disease.[15] The local lesions are likely to be small and to develop slowly, and generalized lesions may not appear at all. A similar observation has been made by Ford and Eliot[16] in transferring the intracellular parasite Bartonella muris to rats. DeMonbreun and I have observed that oral warts of dogs may be delayed or apparently completely inhibited by malnutrition or intercurrent disease.

Such instances as these may well indicate that, on the cytotropic hypothesis, the intracellular medium may become altered by dietary and nutritional deficiency or by chemical means so that the cell becomes less susceptible or less congenial to an intra-virus. The profound modification of epithelia noted by Wolbach[17] in vitamin A deficiency and the experiments of MacNider[18] and later of Gil-y-Gil[19] on immunity of cells to chemical poisons lend some credence to this view.

Further experiments are needed in this direction. Especially is it important for investigations to be undertaken in attempts to alter the cellular media by chemical means in the hope of modifying the course of an infection by viruses or of preventing infection completely by rendering normally susceptible cells artificially

insusceptible or hypersensitive to the penetration or growth of virus within them. The effects of maturation, differentiation, de-differentiation and metaplasia of cells on their susceptibility to viruses offer especially interesting problems to be studied experimentally.

In summary it has been my effort to emphasize certain contrasts between the pathogenesis of infections due to extracellular parasites and those due to obligate intracellular parasites, and to correlate some of the phenomena of virus infections with those of the latter group, pointing out some implications which suggest definite lines for further investigations in the study of pathogenesis of virus diseases. A better understanding of virus and obligate intracellular parasitic infections will require, in my opinion, a different means of approach and a different background of experimental hypothesis from those applied to the study of extracellular parasites. The present structure of bacteriology and immunology has been built upon a foundation of fact derived largely from studies of those infections which are due to parasites of the free fluid of the body. We must deal now with the agents which reproduce within the living cells of the host.

This is a more difficult group to investigate and to understand, for it is a striking fact that the intracellular parasites and viruses, certainly for the most part, resist cultivation outside their natural environment. They must at present be approached indirectly. One must laboriously investigate all the varied phenomena of pathogenesis, and the protective and immunity responses of the host, contrasting these with the facts and hypotheses available from many years of research into the behavior of parasite and host in their struggle within the body fluids.

REFERENCES

1. Koch, R.: Investigations Into the Etiology of Traumatic Infective Diseases. The New Sydenham Society, vol. **88**, 1880.
2. Metchnikoff, E.: Lectures on Comparative Pathology of Inflammation, 1893.
3. Arkwright, J. A.: Virulence of the Micro-organism in Infective Disease. Lancet, **2**:963, 1929.
4. Rous, P.; and Jones, F. S.: The Protection of Pathogenic Micro-organisms by Living Tissue Cells. Jour. Exper. Med., **23**:603, 1916.
5. Aschoff, L.: Lectures on Pathology. Hoeber, 1924.
6. Pinkerton, H.; and Hass, G. M.: Intranuclear Rickettsiae in Spotted Fever Studied in Tissue Culture. Jour. Exper. Med., **56**:151, 1932.
7. DeMonbreun, W. A.: The Cultivation and Cultural Characteristics of Darling's Histoplasma Capsulatum. Amer. Jour. Trop. Med., **14**:93, 1934.
8. Tyzzer, E. E.: A Fatal Disease of the Japanese Waltzing Mouse Caused by a Spore-bearing Bacillus (Bacillus piliformis, N.S.P.). Jour. Med. Res., **37**:307, 1917-18.
9. Wright J. H.; and Craighead, E. M.: Infectious Motor Paralysis in Young Rabbits. Jour. Exper. Med., **36**:135, 1922.
10. Councilman, W. T.; and Strong, R. P.: Plague-like Infections in Rodents. Trans. Assn. Amer. Phys., **36**:135, 1921.
11. Smith, T.: Parasitism and Disease. Princeton Univ. Press, 1934.
12. Andrews, C. H.: Immunity in Virus Diseases. Lancet, **1**: 989, 1046, 1931.
13. Goodpasture, E. W.: Etilogical Problems in the Study of Filterable Virus Diseases. Harvey Lectures, 1929-30.
14. Stanley, W. M.: Isolation of a Crystalline Protein Possessing the Properties of Tobacco-Mosaic Virus. Science, **81**:644, 1935.
15. Maitland, H. B.; and Scott, W. M.: Bacteria in Relation to Disease. A System of Bacteriology, **6**:20, 1931.
16. Ford, W. W.; and Eliot, C. P.: The Transfer of Rat Anemia to Normal Animals. Jour. Exper. Med., **48**:475, 1928.
17. Wolbach, S. B.; and Howe, P.: Vitamin A Deficiency in the Guinea Pig. Arch. Path., **5**:239, 1928.
18. MacNider, W. deB.: The Resistance of Fixed Tissue Cells to the Toxic Action of Certain Chemical Substances. Science, 81:—, 1935.
19. Gil-y-Gil, C.: Die Immunitat in Nierenepithelgewebe. Ziegler's Beitrage, **72**:—, 1924.

EPIDEMIOLOGICAL PRINCIPLES*

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"Theory, like mist on eyeglass, obscures facts."—*From Charlie Chan in Egypt.*

In undertaking a discussion of epidemiological principles we should have a sort of common footing with respect to the meaning of epidemiology. With this, as with many other words, the times have moved beyond or away from the original meaning. The words that "the Greeks had for it" meant a study of or a treatise on something spreading widely and affecting many persons at the same time. In the present day, however, we do and should apply at times what we call epidemiological studies to one human case of a disease in a large community. Such studies surely would be made intensively if now there were found, for instance, one case of yellow fever in New Orleans, or one case of bubonic plague in St. Louis, or one case of Asiatic cholera in New York. As a working, and perhaps an up-to-date, definition the following is proposed: *Epidemiology is a study of conditions known or reasonably supposed to influence the prevalence of disease.*

Epidemiology, in art and practice, is objective and positive, and it is unrelenting in its factual features. It is a science of facts.

In conducting epidemiological studies certain principles of procedure are essential to success and satisfaction. Among them are the following:

(1) First and foremost and above all else,

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work, and that means hard work and plenty of work.

(2) Patient, painstaking, careful and thorough collection of all available facts which may have any bearing on the situation, and due consideration of every possible factor until the inoperative ones can be eliminated beyond reasonable doubt.

(3) Broad-mindedness and open-mindedness in obtaining and in studying data, and, in conducting interviews to obtain data, avoidance of any tendency to lead witnesses.

(4) Maintenance of a reasonably clear perspective, and refrainment from superficial surmises, from hasty half-baked conclusions and from fixed opinions or efforts to prove something which may not be so, or to marshall facts so that they may tend to support unduly a "hunch" or a preconceived hypothesis or theory before all the salient returns are in.

(5) Assemblage of the data so that they will make a clear-cut, readable picture with first things first and with the foremost facts sufficiently but not unduly emphasized.

(6) Common sense and honesty in the interpretation of the findings so that the facts will compel a reasonable conclusion and not be twisted, distorted or obfuscated so as to be made to appear to support a conclusion perhaps desired but false.

Work.—Among the most common faults of epidemiological investigations is lack of hard, intelligent work. This, among investigators, may be due to innate laziness, to over-confidence in superficial analogies, or to what may be called a sort of "smart aleckism." Since the early days of the medicine men of the primitive tribes, physicians have been popularly supposed to possess much knowledge and wisdom. In consequence, some of them appear disposed sometimes to make a pretense at knowledge, diagnostic, therapeutic or epidemiological, which they have not. Doctors, even as other persons, of course, when they do not know should realize they do not know and, as a rule, say so, and work to learn. In epidemiology we must not trust to "seeing through a glass darkly." We must work to collect and to see the facts.

When we know in essential detail the rates of distribution of an outbreak of disease we can begin to see light. To learn the distribution we must locate the cases and go to the homes of all or at least a fair proportion of them and by interviewing the families painstakingly, patiently and pleasantly try to ascertain every salient fact about differences in antecedent conditions between those affected and those not affected by the disease. This is tedious, and at times actually boring hard work, but experience teaches it is necessary and that it is much more important than any other one thing which can be done in an epidemiological study. We must determine and express in rates as nearly exactly as may be practicable the regional (or geographical) distribution, the age-sex-race distribution, and (when appropriate) the distribution with respect to social and economic and environmental sanitary conditions, to seasonal climatic conditions, to water supplies, to milk and other food supplies, to exposure to insects, vermin and other animals which appear as possible vectors or harbors of the infection, to personal contact (direct or indirect) with human cases of the disease or with possible human carriers of the infection, and to exposure to contaminated, and possibly infected, clothing or other inanimate things.

Facts.—Facts are obstinate things and, often, are disagreeable things; but to the true epidemiologist they are sacred.

In interviews at the homes of cases much care and patience must be exercised to bring out the truth. In an outbreak of typhoid fever caused by milk-borne infection in Norfolk, Virginia, some years ago, the ascertainment of the date on a pill box at a home led to the determination of the human source of the infection. In a typhoid fever epidemic caused by oyster-borne infection in 13 American cities in the winter of 1924-25,[1] a second visit with careful interviewing at the homes of some of the cases and at some of the restaurants developed facts which had been missed on the first visit, and which established the outbreak in Washington, D. C., as a part of the epidemic. In a typhoid fever outbreak caused by ice cream-borne infection in Chattanooga, Tennessee, in 1917,[2] revisits to homes of cases and further questioning of families brought out positive instead of the negative histories obtained on the first interviews with respect to the eating and the true source of the ice cream eaten, and thereby helped essentially in dissolving the mystery.

Broad-Mindedness and Open-Mindedness.—In the late nineties yellow fever was still a great unsolved epidemiological problem.[3] Numerous theories were in vogue as to the causation and modes of spread. The authorities appeared

broad-minded but not entirely open-minded about the problem. Carlos Finlay's transmission of the infection by means of mosquitoes had been "disproven," and the scientific world generally proclaimed that the mosquito was "out." Neophytes entering the yellow fever epidemiological field in the outbreaks of 1897 and 1898 in the United States were just about ordered by their elders to leave mosquitoes out of consideration as a possible factor. In 1900, however, the genius of Walter Reed put together one and one: (1) the findings of Ross and others with regard to the mode of spread of malaria; and (2) the establishment by Henry Carter of the period of extrinsic incubation of yellow fever. Reed then applied, in high degree, work and common sense. He and his coworkers cut the Gordian knot and liberated forces which removed from almost the entire world the terrors of this "pestilence which walked in the night."

Chatin,[4] a French physician, established as early as 1852 that iodine content in water, food and soils was low in regions in which endemic goiter was common. His work unfortunately was discredited by the then authorities and further advance in the knowledge of this disease was blocked for forty-five years, and practical measures for the prevention of the disease were delayed until the work of Kimball and others in 1917.[5]

William Budd,[6] a country physician in England, by hard work, by careful and thorough observation, and by remarkably logical deduction, established and presented as early as 1857 nearly all of the knowledge we have today about the epidemiology of typhoid fever. Murchinson's pythogenic theory of the causation of this disease, however, then held sway in the mind of the medical profession and Budd's great work was not duly recognized until many years afterwards.[7] Budd also developed about the same time and presented in 1867 most that is now generally accepted as to the causation and modes of spread of tuberculosis;[8] but for years thereafter the medical profession generally held and proclaimed that the disease was hereditary and thereby cast unnecessarily the shadows of grief and fear upon the hearts of many people. William Budd was a great man. As a delayed but deserved and fitting tribute to him, we now might designate him "the father of modern epidemiology."

Perspective.—A notable example of clear perspective in epidemiology was presented in the early studies by Goldberger[9] and his coworkers on the causation of pellagra. Those studies were begun when the scientific world was in a maze of theories and doubts regarding the problem. In fact, it seemed that the doubters had eliminated just about everything except the occurrence of the disease itself. Goldberger worked. He collected facts. He used common sense. He saw the light.

In 1927 a terrific outbreak of typhoid fever occurred in Montreal, Canada. The medium of infection was one of the large milk supplies of the city. All of the milk distributed from the implicated plant was said to be pasteurized. Some of the investigators with apparently a high scientific turn of mind went about with hand lenses looking for finger prints on rubber gaskets and other parts of the machinery in the plant and finally presented a conclusion that the infection had been introduced into the milk by the fingers of the foreman of the plant, who had been found to be a "carrier." Unfortunately, a second outbreak, or a second large wave of the outbreak, occurred after this "carrier" had been removed from the plant for a period too long for him to have had any connection with the causation of the second wave of the outbreak. Others of the investigators considered the following points of evidence: (1) the occurrence of over 4,000 cases of typhoid fever within two periods of a few weeks among the consumers of milk from one supply meant a large volume or frequent heavy dosage of infection; (2) the milk was kept cold from the time it entered the city plant to the time it was distributed to the consumers; (3) the pasteurizing machinery was efficient but not adequate or not operated so as to pasteurize more than about three-fourths of the volume of milk distributed from the plant during the causation periods of the outbreak; and (4) there was ample opportunity for typhoid infection to gain entrance to the milk both at many of the farm sources and at some of the collecting depots outside the city. These investigators established, at least to their own satisfaction, that the infection gained entrance to the milk at some of the farm sources and perhaps also at some of the collecting depots, multiplied therein before the milk was cooled, and went through the city plant in the approximately 25 per cent of the supply which passed through the city plant without being pasteurized.[10]

Picturing.—When a conclusion from epidem-

iological studies is reached, the facts should be marshaled so as to make a clear-cut picture and the conclusion should be timed and presented so as to be convincing to all unbiased and reasonable persons concerned.

Picturing also is important in developing a diagnosis in an epidemiological situation. Of a recent outbreak of typhoid fever in Minneapolis, Minnesota, very careful and thorough epidemiological studies were made. The evidence pointed strongly to the city water supply as the medium of the infection. During the causation period of the outbreak, however, that water supply had been found, so far as the occasional bacteriological examinations of tap samples indicated, to have been well within the accepted standards of water purity. The picture was not complete. Finally, a map was made showing the population of the city by districts in the areas supplied separately by water from each of the two filtration plants and the locations of the homes of the typhoid cases were spotted thereon. This picture showed that the incidence rate of the disease was ten times as high in one of the water areas as it was in the other and, along with all the other facts collected, helped to establish beyond reasonable doubt that the medium of the infection was the water distributed from one of the filtration plants.

Common Sense.—Some iconoclasts insist that common sense is rather rare among our learned. Rare or not, the epidemiologist must have it and use it in full measure or eventually fall by the wayside.

In epidemiological studies of diseases about the causation of which little is known, the exercise of common sense, broad-mindedness and open-mindedness is all important. Hasty conclusions or near conclusions and superficial surmises should be avoided. Semblances of analogy should not be stressed unduly. Work should be done, facts collected, and common sense used.

Of such diseases, two may be mentioned as examples. Some of us do and all of us should admit that as yet little, if anything, is definitely known about the etiology and the epidemiology of encephalitis and poliomyelitis. Outbreaks of these diseases in recent years in the United States have aroused keen and broad interest. Their epidemiological manifestations are exceedingly interesting and puzzling.

Infectious Encephalitis (Type B).—In the late summer and early autumn of 1933 a serious outbreak of encephalitis occurred in Missouri and neighboring states. Clinically, pathologically and epidemiologically it appeared to be a new disease in the United States. It did not spread radially nor uniformly along lines of human traffic, but it "jumped" from area to area or just occurred in different areas, as a rule, many miles apart. It attacked mainly middle-aged and elderly persons. Such age group distribution suggested a lack of community immunity. The incidence rate of the disease was three times as high in St. Louis County as in St. Louis City, and over four times as high in the Independence (Missouri) region as in the St. Louis region. In St. Louis City the rate was much higher (over four times) in the outlying western wards than in the densely populated downtown most eastern wards. In the ten Missouri counties nearest St. Louis County, with an aggregate population of about 190,000, only eight cases were reported. The city of East St. Louis had comparatively few cases. Chicago escaped entirely. Louisville had a considerable outbreak. Kansas City was lightly stricken. Jefferson City and Sedalia, on the main line of traffic between St. Louis and Kansas City, escaped, while Columbia, offside from the main current of travel, had a rather high incidence. Two possible factors in the spread of the disease were given especial attention: (a) personal contact and (b) mosquitoes. The reports as yet published on the intensive and extensive epidemiological studies which were made appear quite fragmentary. Positive or even suggestive evidence of conveyance by personal contact was amazingly lacking. The conclusion, or the near conclusion, however, which has had the most official support is this:[11]

> "As regards communities, the spread by contagion, in the broadest sense of the word, presumably by human transfer, is obvious, but as regards individuals, the reverse is true."

From observations made by some of the investigators,[12] it appeared (1) that the outbreaks occurred only in areas which were infested to an unusually large degree with mosquitoes of one species (Culex pipiens) which had bred in nearby creeks and streams heavily polluted with sewage; (2) that large and populous areas, without that set of conditions, situated between the affected areas, entirely or nearly escaped; and (3) that the cases of the disease generally occurred in perscns who, during the four weeks prior to illness, were especially exposed to the bites of such mosquitoes. The negative results from the very limited and specifically condi-

tioned experiments to convey the infection by mosquitoes from person to person, of course, have not any epidemiological or etiological significance. In this connection the recent work by Merrell, Tenbroek, Hurst and Traub[13] on equine encephalomyelitis and that by Webster, Clow and Bauer[14] with the "St. Louis type of encephalitis virus" are exceedingly interesting.

In view of all the facts, surmises, hypotheses and theories recorded to date regarding infectious encephalitis (Type B), it seems that in future epidemiological studies of this mysterious malady broad-mindedness, open-mindedness and common sense will be highly in order.

Poliomyelitis.—Some gifted satirist well might write a book entitled, "Poliomyelitis, the Doctor's Folly." There is no other disease or group of diseases of common occurrence in recent times regarding which physicians appear to go wrong so much and so often. About this problem, and it is a mighty problem, etiologically, pathologically, clinically, therapeutically, and epidemiologically, some doctors say little or nothing and try to look wise; some say much and demonstrate a lack of wisdom; some, especially among beginning students, rush in with wild enthusiasm and manifest every form of mild insanity known to psychiatry, and some, especially among the long-time students, and these in some instances are the most hopeless ones, appear to develop what may be called a sort of cerebral ossification.

Poliomyelitis strikes terror to the hearts of loved and loving parents of little children. Due to the popular dread and ignorance of it, it furnishes a notably fertile field for mercenary charlatanism and quackery. Most of us who have been through outbreaks could cite in this connection startling instances of man's inhumanity to man. We physicians have little or no satisfactorily definite knowledge about what we call poliomyelitis. We should be honest and say so. When we advocate what we hope will prove effective therapeutic or preventive measures, we should be frank and admit the measures are experimental.

A recent officially approved report presents without a "perhaps" or even a "probably" items with respect to etiological agent, source of infection and mode of transmission of poliomyelitis.[15] Those items as set forth in that report are impressively positive, but to some of us, perhaps, not entirely convincing.

Learned physicians do disagree about the nature and the mode of invasion of the etiological agent.[16] Some hold that it is an ultra-microscopic filterable virus, some hold that it is a culturable and microscopically visible bacterium, and others, perhaps with a happy spirit of compromise, hold that in one phase it is a culturally and microscopically readily demonstrable micro-organism and in another phase an ultramicroscopic filterable virus, a sort of now you see it and now you don't proposition, if you please.

Some of the therapists who advocate curative serums or heroic surgical measures state that the remedy, to be fully effective, must be administered within the first day or two of systemic symptoms and before paralysis develops. Of course, if a considerable number of early stage cases of illness were erroneously diagnosed as poliomyelitis and were so treated, the remedy might obtain, at least among the more gullible, a high rating. The position taken in the officially approved report[15] above cited that only paralytic cases should be counted officially as poliomyelitis seems well founded and practically applicable in epidemiological studies.

There should be among rational students of the problem no doubting that there is serious need for much more positive knowledge than we yet have about the epidemiology of poliomyelitis. Different outbreaks present many most remarkable vagaries. In epidemiological manifestations, the outbreak in the Los Angeles, California, region last year, judging by the fragmentary reports[17] on it, appeared as different from the outbreak in Louisville, Kentucky,[18] this year as an outbreak of measles appears different from an outbreak of bubonic plague. Is it possible that what we call poliomyelitis is really two or more diseases caused by different agents spread in different ways? Imagine the confusion an epidemiologist of earlier days, before typhus and typhoid fevers were differentiated, would have had in studying different and widely differing outbreaks of what then were regarded as one disease called continued or typhus fever. Perhaps we have in this an actual epidemiological analogy.

In view of the whole situation, it is certain that future epidemiological studies of poliomyelitis should be made with humility, with honesty, with broad-mindedness and open-mindedness and with as much sanity as possibly can be retained.

CONCLUSION

Among the essentials to success in epidemiology are: (1) hard and patient work; (2) careful and thorough, unbiased collection of facts; (3) broad-mindedness and open-mindedness in the collection and in the study of data; (4) clear perspective in considering the general features of situations; (5) assemblage of data so as to make a definite and readily readable picture; and (6) common sense in interpreting and in presenting the findings; and the greatest of these are work and common sense.

REFERENCES

1. Supplement No. 50 to the Public Health Reports, 1925.
2. Lumsden, L. L.: The Determination of Ice Cream as a Factor in the Spread of Typhoid Fever Infection. Amer. Jour. Public Health, **7**:1005 (Dec). 1917.
3. Public Health Bulletin No. 4: Yellow Fever: Nature, Diagnosis, Treatment and Prevention, 1898.
4. Marine, David: J.A.M.A., **104**:2338 (June 29) 1935.
5. Marine, David; and Kimball, O. P.: Jour. Lab. & Clin. Med., **3**:40 (Oct.) 1917.
6. Budd, William: Typhoid Fever. London, 1873.
7. Whipple, George C.: Typhoid Fever, 27-36. (Introductory Essay by William T. Sedgwick.) New York, 1908. Freeman, Allen W.; and Lumsden, L. L.: Typhoid Fever in Rural Virginia. Amer Jour. Public Health, **2**:240-252, 1912.
8. Budd, William: Lancet, **2**:451-452 (Oct. 12) 1867.
9. Goldberger, *et al.*: Public Health Reports, Washington, pp. 1683-1686, June 26, 1914. Reprint No. 307 from the Public Health Reports, **30**: No. 43 (Oct. 22) 1915.
10. Lumsden, L. L.; Leake, J. P.; Crohurst, H. R.; and Waller, C. E.: Unpublished official report, 1927.
11. Public Health Bulletin No. 214, p. 25, and J.A.M.A., —: 7:30 (Sept. 8) 1934.
12. Lumsden, L. L.: Unpublished official report, 1933.
13. Merrell, Tenbroek, Hurst and Traub: Jour. Exper. Med., **62**: 677-685 and 687-695 (Nov. 1) 1935.
14. Webster, Clow and Bauer: Jour Exper. Med., **61**:479-487 (April 1) 1935.
15. Public Health Reports. **50**:1044-1045 (Aug. 9) 1935.
16. Landon, John F.; and Smith, Lawrence W.: Poliomyelitis, pp. 9-14, 23-29 and 67-71, **7**:270-290 (Aug.) 1935. New York, 1934.
17. Amer. Jour. Public Health. **24**: No. 12 (Dec.) 1934.
18. Lumsden, L. L.: Official report in course of preparation.

DISCUSSION (*Abstract*)

Dr. C. H. Halliday, Baltimore, Md.—Interested as I am in medical history in general and public health history in particular, it may not be amiss to mention here that Dr. Lumsden was one of the first physicians to receive the title of epidemiologist. Dr. Hill, I believe, was the first physician to be officially designated as an epidemiologist by the State of Minnesota.

In my limited experience it has been my pleasure to follow Dr. Lumsden in his field of investigation. In each instance where I have adhered to the principles laid down by him in his paper, I have been successful in solving the problem.

As a physician is interested in the clinical reaction between an invading micro-organism in an individual; the epidemiologist studies the reaction around a group of individuals. This mass reaction is characterized by a certain fairly defined distribution of cases with regard to time, age, sex, occupation and hygienic surroundings.

Epidemiology is so closely associated with bacteriology, immunology, pathology and statistics that they cannot very well be separated. The epidemiology rests principally upon the collection and analysis of all available data in such a way as to offer the broadest perspective with regard to the nature and mode of spread of the disease.

The knowledge of the epidemiology of a disease implies knowledge of all the conditions in nature under which disease occurs and it could follow also that it implies knowledge of conditions under which disease does not occur. The inquiry into the endemic expression of disease must be more intensively investigated and the incurrent conditions and the reasons for their maintenance between epidemics must be investigated. Sound epidemiological data are responsible for much of our accumulated information.

Many important facts and conceptions rest solely or chiefly upon epidemiological investigations. These may be summarized as: the infectious nature and communicability of certain common diseases; immunity resulting from one attack of some diseases; and differences between diseases with respect to season, age distribution, geographical distribution and periodicity.

If the available information is carefully collected and arranged in orderly sequence, the deductions should lead to logical conclusions.

Dr. W. B. Grayson, Little Rock, Ark.—Epidemiological investigation is an important function of any health department, large or small. The idea that epidemiological activities are primarily research in nature, and thus have no practical importance, is wrong. What is epidemiology? There have been several definitions given and the one given by Dr. Lumsden is a good one. If I may add my own, I would call an epidemiologist a scientific investigator of community diseases as regard causes, propagation and prevention. An epidemiologist should possess certain qualifications, among them a knowledge of statistics, epidemics and their history, bacteriology and immunology, community disease rather than individual disease.

Epidemiologic principles might be divided as follows:

(1) Experimental epidemiology, which probably does not hold much interest for the health officer.

(2) Investigation of epidemics, which should be handled by the health officer. He should approach all field problems with an open mind. I think the first thing he should do in investigating an epidemic is to quiet the fears of the people of the community. In epidemics of some diseases, the population is very much alarmed, and he should first quiet its fears. By so doing he will receive intelligent cooperation. Of course, the next thing to do is to make an accurate diagnosis. A mental picture of all the general epidemiological features of the particular disease will help to make a diagnosis.

(3) The third step would probably be the investigation of invasion in the community, and exposures, especially in the home where the disease prevails.

(4) The source of infection and mode of transmission should be determined. After the case is isolated and contact broken, specific prophylactic measures that are in common acceptable use should be established.

A great many times the investigation and solving of a specific epidemic accomplishes much for handling outbreaks of similar nature in the future, but while the problem is being solved a great many deaths occur, a case of locking the barn door after the horse is stolen. I believe in such epidemiological work, of course, but I also believe more can be accomplished by health officers working in a continuous effort in a

day by day determination of sources of infection in a community. The constant searching for contacts of cases of tuberculosis and syphilis, and the discovery of mild types of communicable diseases, such as diphtheria, scarlet fever, or poliomyelitis, will yield far more effective results in prevention of disease than solving of a particular epidemic of severe proportions.

We should train our directors of health units and the private physicians in epidemiologic principles; then they would take more interest in the every day investigation of communicable diseases. The nurses should have a knowledge of epidemiology, as they could aid greatly in the history of community infections and the investigations of outbreaks. Better cooperation could be expected if the laymen were informed of these conditions.

Dr. Lumsden (closing).—In reply to the question, are public health nurses qualified to collect epidemiological data, my answer is yes, provided the nurses selected for such work have the right sort of personal equation, are duly trained in the technic of interviewing, have and use common sense and are conscientious, diligent, pleasant and interested in the performance of the duties. In the course of studies of encephalitis in Missouri in 1933 and of poliomyelitis in Kentucky this year, it was my good fortune to have in each situation the assistance of a public health nurse in whose epidemiological case history taking I had complete confidence. In fact, though I might have been somewhat reluctant to admit it, I thought that those nurses could obtain at the homes of cases the epidemiological data as nearly accurately and completely as I or any other physician or any sanitary engineer well experienced in epidemiological work could obtain them.

DEFICIENCY POLYNEURITIS*

By H. M. WINANS, M.D.,
and
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The polyneuritis of beriberi has been recognized as a deficiency disease for some time. Much more recent, however, is the development of the idea that a similar polyneuritis seen in a variety of other conditions is also due to a deficiency of some type in the diet. The weakness, rapid pulse and cardiac failure associated with the degenerative symptoms in the nervous system have made the idea of an intoxication of some type appear logical. On the other hand, the close association with reduced or altered food intake and disturbances of the gastro-intestinal tract have suggested the conclusion that a deficiency is the chief cause.

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The chief theories may be summarized as follows:

(1) *The Oryzatoxin Theory.*—Teru-Uchi[1] and his associates have claimed that extracts from rice injected into pigeons produce the polyneuritis of beriberi. This extract has been thought to contain some toxin derived either from the rice itself or from a *Bacillus vulgatus* which grows in the interior of certain grains, especially if they are allowed to become moist. This claim has been denied by Simpson,[2] who was unable to confirm the results.

(2) It has been considered that there is some toxin in the pernicious vomiting of pregnancy and other conditions associated with disturbances in the food intake similar in its action to that of lead and other metals. It has been shown by Strauss[3] and Berkwitz and Lufkin,[4] however, that the polyneuritis in these conditions is identical with that observed in deficiency diseases.

(3) Proof is practically complete that the polyneuritis of beriberi, vomiting of pregnancy, and other conditions where there is a food deficiency, is due to the lack of vitamin B_1, although possibly the entire complex enters into it. That the absence of vitamin B in itself is usually not sufficient to cause the development of polyneuritis has been demonstrated by Zimmerman and Burack,[5] who have shown that it may develop in dogs supplied with an adequate amount of B complex but deprived of other food. Mellanby,[6] moreover, believes that the changes in the nerve fibers do not develop until there is a depression of the vitamin A storage in the liver.

The pathologic changes in the nervous system have been shown to be found, not only as degenerative changes of the peripheral nerves and anterior horn cells, but petechial hemorrhages have been demonstrated in the brain and spinal cord. Kinnersley and Peters[7] have shown that polyneuritis of vitamin B_1 deficiency is intimately associated with a localized accumulation of lactic acid of the brain, and Meiklejohn[8] found that concentrates of this vitamin were capable of repairing this defect.

The dependence of the disease upon other factors has also been demonstrated by various observers who have noted its development following postoperative vomiting, operations on the gastro-intestinal tract, colitis, cancer and benign lesions (Christopher,[9] Jones,[10] Barnes[11] and Urmy[12]). In the pregnant woman, Strauss and

Castle[13] have shown that there is a definite depression in the amount of free hydrochloric acid and pepsin secreted and probably other disturbed functions of the gastro-intestinal tract.

In a consideration, therefore, of patients likely to develop polyneuritis, we should expect to find it occurring in those who present a deficient nutritional background due to economic conditions, dietary regimens or alcoholism accompanied by reduced food intake. Under these conditions any prolonged illness accompanied by reduced food consumption might be expected to produce the disease.

While the findings in polyneuritis, once it has developed, are quite definite, it is much more important to recognize the early symptoms which may precede neurological findings for a considerable period of time. Of these, weakness, loss of appetite, dizziness, rapid pulse, numbness and tingling, burning of the soles of the feet or palms of the hands and pyrosis are the most important. Elevation of the pulse rate and diminution of vibratory sense are early physical findings. A curious symptom which has probably not received the attention it deserves is a voice change due to involvement of the recurrent laryngeal branch of the vagus nerve. This was mentioned by Sison[14] and has been noted in several papers since, but without particular emphasis. A survey of the early symptoms, including this voice change, reveals how easily one may mistake most of them for natural weakness and depression due simply to the operation or a period of illness.

The following case exemplifies the development of beriberi during the course of another illness:

Miss H., aged 21, was admitted to Baylor Hospital May 22, 1934, with a tentative diagnosis of rheumatic fever. She showed continued fever with weakness, rapid pulse and loss of appetite. A diagnostic study was made of her condition, the only positive finding being related to the heart, where repeated x-ray studies showed increasing prominence in the left auricular region, although the heart itself was not enlarged. It was the opinion of the roentgenologist that these changes indicated mitral disease.

She was kept at bedrest for three months. During this time great difficulty was experienced in providing sufficient nutriment and on several occasions it was necessary to use a nasal tube. Almost exactly two months after admission, it was noticed that her voice was weak and of a higher pitch.

Neurological examination showed definite foot and wrist drop without complete loss of extensor power. The deep reflexes were absent and there were minimal sensory changes on the distal ends of the extremities. Nerve muscle tenderness was present.

She was given liver extract intramuscularly daily and efforts to increase nutrition were redoubled. Three days later her condition was somewhat worse, but ten days later she was materially improved and at the end of five more days her appetite had increased and there was much less evidence of neurological involvement.

In this patient the polyneuritis developed while she was under close observation. Undoubtedly a greater alertness for the early symptoms would have resulted in treatment before definite physical findings appeared.

As a contrast the following case is reported, although it is impossible to be sure that it definitely represents a deficiency neuritis:

Mrs. P. N. A., aged 57, entered Baylor Hospital December, 1933. Her complaint was of tingling of the arms and legs, weakness of the arms, inability to move the legs, generalized aching, insomnia and loss of appetite of one year, and loss of weight. After an attack of influenza one year previously she had not felt well. Five days before her admission she developed tingling and weakness in the extremities and inability to use her legs; also weakness in the jaw with difficulty in opening the mouth and chewing.

Her past history was negative and aside from the above complaints there was nothing in the present history of importance.

Examination showed a blood pressure of 140/86; pupils sluggish in reaction; and general physical examination negative.

Neurological examination showed bilateral facial palsy, peripheral in type; flaccid paralysis of all four extremities with vasomotor and sensory changes and nerve tenderness; moderate stiffness of the neck and positive Kernig and sphincter incontinence.

Laboratory examination showed urine negative; hemoglobin 85 per cent, red cells 4,530,000, white cells 11,150, polymorphonuclears 77, small lymphocytes 17, large lymphocytes 3, and large mononuclears 3. The blood Wassermann and Kahn were negative. The spinal fluid was clear and under normal pressure. Globulin was negative. There was a slight increase in reduction. The colloidal gold reaction was 0001222100.

Her course was rapidly downward in spite of treatment. She developed abductor paralysis in the larynx and died thirteen days after admission.

There are features of the above case which are not commonly found in deficiency polyneuritis. The meningeal reaction in particular suggested an infection. Since autopsy was refused, it is impossible to come to a definite conclusion. Nevertheless, this patient had a year during which her nutrition was certainly below standard and with the few exceptions noted, she presented most of the findings of a deficiency polyneuritis.

Through the cooperation of Dr. Hannah, of the Obstetrical Department, we were able to study 5 cases of vomiting of pregnancy showing polyneuritis.

These cases were admitted to the hospital through the Outpatient Department. Persistent

vomiting with greatly reduced intake of food had been present in all of them for an average period of 2 months. The symptoms were remarkably alike in all the cases, as were the neurological findings which are summarized below:

The fourth case was not one of pregnancy, although the patient was convinced she was pregnant and was admitted to the Obstetrical Department. The findings in this case were practically identical with those showing pregnancy and would seem to lend weight to the idea that there is no special toxemia responsible for these symptoms. Moreover, one case was worse following spontaneous abortion. The symptoms and findings were identical with other forms of polyneuritis, especially those associated with lack of vitamins, whether the patient was pregnant or not. While the mortality has been reported to be high in many of these cases, there was no mortality in this small series. The clouding of the sensorium and the amount of paralysis and sensory changes, even with the evidence of cord involvement, gave no weight to a poor prognosis. In spite of the evidence of cord involvement, there was no evidence of spinal fluid changes in two of the cases.

The clinical history of the above cases showed that an average time of two months of undernutrition was necessary for the development of definite symptoms. Again it is possible that a closer analysis might have demonstrated the beginning of trouble much earlier. The similarity of findings in all of the cases is striking. In four of the five cases voice change indicating laryngeal disturbance was a definite finding.

Treatment is naturally directed toward the administration of an adequate diet. If vomiting and nausea are pronounced, it is best to withhold food and fluids by mouth for 24 to 48 hours and give glucose intravenously together with saline by hypodermoclysis. Liver extract should be given intramuscularly daily from the beginning, since this provides a simple method of administration of the vitamin B complex. As soon as possible the patients are put on a high vitamin diet.*

Brewer's yeast may be added to this and as the appetite returns, liver extract may be administered in capsules instead of by hypodermic. The response to intramuscular liver extract in many cases is as gratifying as that seen in deficiency anemias. The patient's appetite and ability to take food frequently improves within a few days and there is an evident return of strength before the increased intake of food could be wholly responsible.

CONCLUSIONS

The nutritional background of a considerable portion of the population is such as to provide for the development of deficiency polyneuritis under a variety of conditions. Marked changes

*The following represents the minimum intake in twenty-four hours. The patients are encouraged to eat as much as possible beyond this minimum: Orange juice, 500 c. c.; tomato juice, 500 c. c.; green vegetables, 500 gms.; eggs, 2; milk, 1,000 c. c.; cream, 250 c. c.; beef, 180 gms.; whole wheat bread, 200 gms.; butter, 25 gms.

VOMITING OF PREGNANCY WITH POLYNEURITIS

	Case 1	Case 2	Case 3	Case 4	Case 5
Sensorium	Cloudy	Clear	Clear	Clear	Clouded
Larynx	Voice weakness	Voice high pitched	Strangling	Strangling	0
Meningeal reactions	Negative	Negative	Negative	Negative	Negative
Cranial nerves	Negative except 10th	Negative except 10th	Negative except 9th and 10th	Negative except 10th	0
Tactile discrimination	Reduced	Reduced+++	++++	+++	++++
Vibratory sense	Normal	Lost in feet	0	Reduced	Lost in hands and feet
Position sense	Normal	Lost in feet	0	Normal	Intact
Deep reflexes	Exaggerated	Abolished	Absent	Present	Intact
Babinski	0	0	0	0	0
Muscle weakness					
Extensors	++	+++	++++	++++	+++
Flexors	0	+++	++++	+++	+
Wrist drop	0	++	++++	++	0
Foot drop	+	++	++++	++	0
Ataxia	+	+++	+++	++	+++
Atrophy	0	+	+++	0	0
Sphincter involvement	0	0	0	0	0
Trophic changes	+	++	++	0	++
Tenderness	++	++++	++++	++++	+++

in the diet may decrease the intake of the vitamin B complex below the necessary minimum. Alcoholism, intestinal operations and prolonged gastro-intestinal upsets, including the vomiting of pregnancy, may all serve to develop this disease. In any continued illness associated with loss of appetite, the possibility of the development of polyneuritis must be borne in mind. In addition to the usual findings, changes in the voice are particularly significant and may provide an early clue to the diagnosis.

BIBLIOGRAPHY

1. Teruuchi, Y.; Oyama, T.; Nakamura, K.; and Wada, C.: On Mode of Action of Vitamin B; (Aetiology of Beriberi). Japan Med. World, **9**:309-312, Oct., 1929.
2. Simpson, A.: Studies in Vitamin B_1. (Part II. The Oryzatoxin Theory.) Bull. Inst. Med. Research, Fed. Malay States, No. 1, 1934.
3. Strauss, M. B.: The Etiology of "Alcoholic" Polyneuritis. Amer. Jour. Med. Sci., **189**:378-382, March, 1935.
4. Berkwitz, N. J.; and Lufkin, N. H.: Toxic Neuronitis of Pregnancy. Surg., Gyn. & Obst., **54**:743-757, May, 1932.
5. Zimmerman, H. M.; and Burack, Ethel: Lesions of the Nervous System Resulting from Deficiency of the Vitamin B Complex. Proc. Soc. Exper. Biol. & Med., **28**:645, March, 1931.
6. Mellanby, Edward: The Experimental Production and Prevention of Degeneration in the Spinal Cord. Brain, **54**: 247-290, Part 3, Sept. 1931.
7. Kinnersley, H. W.; and Peters, R. A.: Carbohydrate Metabolism in Birds: Brain Localization of Lactic Acidosis in Avitaminosis B and Its Relation to Origin of Symptoms. Biochem. Jour., **24**:711-722, 1930.
8. Meiklejohn, A. P.: Avian Polyneuritis. The Biochem. Jour., **27**:1310-1320, 1933.
9. Christopher, F.; Paskind, H.; and Snorf, L. D.: Multiple Neuritis Following Biliary Tract Operations. Amer. Jour. Surg., **22**:280-283, Nov., 1933.
10. Jones, Chester M.: Peripheral Complications of Ulcerative Colitis. Med. Clin. N. Amer., **16**:919-928, Jan., 1933.
11. Barnes, J. M.: Typical Pellagra Syndrome Developing in Patient with Chronic Ulcerative Colitis while under Hospital Treatment. Ann. Clin. Med., **4**:552, Jan., 1926.
12. Urmy, T. V., et al.: Beriberi Secondary to Short-Circuited Small Intestine. N. Eng. Jour. Med., **210**:251-254, Feb. 1, 1934.
13. Strauss, M. B.; and Castle, W. B.: Studies of Anemia in Pregnancy. Amer. Jour. Med. Sci., **184**:655-673, Nov., 1932.
14. Sison, Antonio: Osler's Modern Med., **2**:815, 1925.

DISCUSSION (*Abstract*)

Dr. Hugh J. Morgan, Nashville, Tenn.—The Section is fortunate in having had this important subject brought before it. In a recent valuable contribution by Cobb and Coggeshall a working classification of the neuritides is offered as follows:

(1) Virus neuritides, including the neuritis occurring in association with poliomyelitis, encephalomyelitis, epidemic encephalitis, "Landry's paralysis," mumps, and so on.

(2) Bacterio-toxic neuritides which occur with diphtheria, streptococcus infections, typhoid, and so forth.

(3) Chemical neuritides, the best known of which are: lead, arsenic, and tricresolphosphate.

(4) Deficiency or metabolic neuritides.

Dr. Winans' interest lies in the last group. It is interesting that we include here not only the neuritides of beriberi, pernicious anemia, pellagra, sprue, but also the peripheral nerve lesions associated with chronic wasting diseases, chronic colitis, and toxemia of pregnancy.

The therapeutic implications of Dr. Winans' presentation are timely and important.

THE STOMACH AND ANEMIAS*

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The newer classifications of the anemias take into account the more recent knowledge of hemoglobin and red cell formation. They destroy the old idea that anemias can be easily divided into primary anemias and secondary anemias. The classification that I propose to follow is based on the cause, and therefore gives a clue as to the specific treatment to be followed. It is a classification on the basis of therapeutics and shows the anemias divided in the following manner:

(1) Deficiency anemias
(2) Myelogenic anemias
(3) Erythroclastic anemias

These three types with their main divisions and subdivisions are given below:

(1) DEFICIENCY ANEMIAS

(A) *Anemias Related to the Anti-Anemia Factor Found in Liver and Specific in the Treatment of Pernicious Anemia.*—(1) Anemia may be due to absence from the diet of the anti-anemia factor. This type is called primary or exogenous macrocytic hyperchromic anemia. Examples are: pernicious anemia, sprue, pernicious anemia of pregnancy, and the anemia of pellagra.

Pernicious anemia is the most common form of macrocytic hyperchromic anemia. Since the anti-anemia factor is necessary in the production of red cells, we find a shortage of these red cells in this type. To compensate for the small number of red cells, those present in the blood stream are large cells (macrocytic, ten to twelve microns) and rich in pigment (hyperchromic). The anemia is called exogenous, since it is caused by the failure to provide a proper intake of the anti-anemia factor in food material coming from the outside, or the failure of the stomach to digest or absorb.

The anti-anemia factor consists of an intrinsic principle found in stomach tissue and an extrinsic principle derived from the food intake. The extrinsic principle is believed by some investigators to be vitamin G, or the anti-pellagra vitamin. Other investigators doubt the identity

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of the extrinsic principle with vitamin G. The intrinsic principle produced in the stomach wall combines with the extrinsic food principle to produce the anti-anemia factor, an excess of which is stored in the liver. Liver extract is believed to contain a combination of the intrinsic and the extrinsic principle.

There are two types of anemia, depending upon the absence of one of the principles in the anti-anemia factor found in liver. Type 1 is due to the absence of the intrinsic principle found in the stomach tissue. An example of this type is pernicious anemia. Type 2 is due to the absence of the extrinsic principle found in food, which was erroneously thought to be vitamin G. Some cases of sprue constitute examples of this type.

(2) Anemia due to defective production or faulty assimilation of the anti-anemia or anemia-preventing factor is known as secondary or endogenous hyperchromic anemia. Examples are: sprue, anemia due to pregnancy, anemia due to anastomoses, anemia due to gastric carcinoma, anemia due to Bothriocephalus latus infestation, and pernicious anemia of pregnancy (increased demand or relative insufficiency).

(B) *Anemias Related to Iron Deficiency.*—This type is called microcytic hypochromic anemia. The cells are small (five microns or less) and poorly pigmented, due to a deficiency in hemoglobin. Hypochromic anemia may or may not be accompanied by achlorhydria. The type may be subdivided into:

(1) Anemia due to insufficiency of iron in the food intake. This type is called primary or exogenous microcytic hypochromic anemia. Examples are: chlorosis, anemia of premature infants, and milk anemia.

(2) *Anemia Due to Loss of Iron.*—This type is called secondary or endogenous microcytic hypochromic anemia. There are two types of this particular form. Type 1 is anemia due to loss of iron through hemorrhage due to menorrhagia, peptic ulcer, pulmonary hemorrhage, scurvy, trauma, *et cetera*. Type 2 includes the anemias due to loss of iron through failure of intestinal absorption. Examples are: sprue, chronic diarrhea, celiac disease, small intestinal stenosis, gastric hypo-acidity or anacidity as in fevers, infections, metabolic diseases and gastric disturbances, and high protein diet neutralizing the free acid of the stomach. Anemias due to lack of vitamins may, among other things, be the result of loss of iron.

Beriberi, pellagra, scurvy, rickets, celiac disease and acrodynia are the result of vitamin deficiencies. Hypo-acidity or anacidity accompanying avitaminoses, as well as constipation or diarrhea and other gastro-intestinal upsets, aid in producing anemia through malabsorption.

(3) Anemia due to faulty assimilation of iron is also a secondary or endogenous microcytic hypochromic anemia. Anemia due to loss of digestive fluids belongs to this class which is subdivided into anemia due to loss of bile (bile fistula) and that due to loss of pancreatic secretion (pancreatic or duodenal fistula).

(C) *Anemia Related to Copper Deficiency.*—Iron cannot be used to build hemoglobin unless copper is present as a catalytic agent. Deficiency in copper therefore causes a tendency to poor assimilation of iron.

Milk anemia occurs in infants and children, in experimental animals and in patients subsisting largely on milk or milk products. Milk and cream form the basis of therapeutic diets in gastric or duodenal ulcer, in idiopathic epilepsy and in fevers. Milk is poor in iron, in copper and in the anti-anemia factor efficient in the treatment of pernicious anemia (macrocytic hyperchromic anemia).

(D) *Anemia Related to Protein Deficiency.*—(1) Anemia may be due to low protein intake, as in famine, hunger or war edema.

(2) It may be related to faulty assimilation of protein as in nephrosis.

(E) *Anemia Related to Vitamin G Deficiency.*—This anemia is a specific anemia relieved only when vitamin G (Brewer's yeast) is administered, provided all other anti-anemia factors are included in the diet or administered as medication.

(F) *Anemia Related to Vitamin C Deficiency.*—This anemia is a specific anemia relieved only when vitamin C is administered, provided all other anti-anemia factors are included in the diet or administered as medication.

(G) *Anemia Related to Thyroid Deficiency.*—This anemia is a specific type relieved only by the administration of thyroid substance, provided all other anti-anemia factors are included in the diet or administered as medication.

FACTORS IN THE DIAGNOSIS OF ANEMIA

In the diagnosis of any type of anemia we must take into consideration, first, the quantity

of hemoglobin in the blood; second, the number of red cells; third, the size of the individual red cell; and fourth, the amount of pigment in the individual cell.

From the standpoint of size we may divide erythrocytes into normocytes, microcytes and macrocytes. From the standpoint of pigment content, we may regard erythrocytes as normochromes, hypochromes and hyperchromes.

We may classify anemias on the basis of the size and pigment content of the red cells into six different types:

(1) Normocytic normochromic anemia
(2) Normocytic hypochromic anemia
(3) Microcytic hypochromic anemia
(4) Macrocytic normochromic anemia
(5) Macrocytic hypochromic anemia
(6) Macrocytic hyperchromic anemia

In the anemia caused by acute hemorrhage there may be a reduction in the number of cells while those remaining are normal in size and hemoglobin content (normocytic normochromic anemia). If the acute hemorrhage is sufficient to produce an iron deficiency, we have a hypochromic normocytic anemia, and eventually a hypochromic microcytic anemia.

STOMACH AND INTESTINE

Gastrin.—The secretion of gastric juice following the ingestion of a meal is due only in part to a humoral mechanism. That a humoral mechanism is concerned has been demonstrated by the secretion of an auto-transplanted gastric pouch following a meal. The humoral agent or agents may be either absorbed secretagogues present in or arising from the digestion of certain foods (meat, liver or other substances) or the hormone gastrin.

The fraction of liver extract that contains the anti-pernicious anemia substance is rich in gastric secretagogic potency. This fraction stimulates gastric secretion on local application to the gastric and intestinal mucosa. It does not act by being absorbed from the stomach, but may act by being absorbed from the intestine. If this fraction is freed of vasodepressor substances, it will stimulate gastric secretion when slowly injected intravenously. Thus, there is an example of a gastric secretagogue that may act by way of a humoral route. The hormone gastrin is supposed to be elaborated chiefly by the mucosa of the pyloric antrum, and possibly by the mucosa of the intestine, when the mucosa is appropriately stimulated, preferably by solutions containing secretagogues.

Secretin.—The discovery of secretin by Bayliss and Starling in 1903 is one of the milestones in endocrinology. In the description of their observations they coined the term hormone. They found that when dilute acid is applied to the mucosa of the upper part of the intestine the pancreas is stimulated to secrete its digestive juice. They also showed that the intravenous administration of acid extracts of the duodenal mucosa stimulated pancreatic secretion. It was later demonstrated that application of acid to a transplanted jejunal loop will cause the transplanted tail of the pancreas to secrete; if the circulation of two dogs is cross-connected and acid is then placed in the duodenum of one of the pair, the pancreases of both will be stimulated to secrete.

It should not be surmised from these crucial experiments that acid is the only substance that causes secretion to be formed. Fatty acids, soaps and peptones are other food substances that cause the duodenum to elaborate secretin. All attempts to demonstrate that postabsorptive circulating substances originating from food are concerned in stimulating the pancreas to secrete have met with failure.

Highly purified preparations of secretin have a slight cholagogic and diuretic effect, which is of no practical significance. Similar preparations have no effect on sugar metabolism. The isolation of secretin in crystalline form has recently been reported.

Highly purified preparations of secretin have been injected intravenously into man for the purpose of ascertaining whether secretin is of practical use for estimating pancreatic function. It is too early to state whether secretin will be of value in this regard. Secretin has no known therapeutic value. It is ineffective when taken by mouth, and it is relatively inactive hypodermically.

Cholecystokinin.—The chief stimulus of gallbladder contraction thus far discovered is the hormone cholecystokinin. Stimulation of autonomic nerves in the cat or dog has never been observed to have more than a slight temporary effect on the gallbladder. Attempts to demonstrate that postabsorptive circulating fatty sub-

stances originating from food are concerned in gallbladder evacuation have met with failure.

Enterogastrone.—It has long been known that undigested fat inhibits gastric secretion and motility, particularly when the fat is in the intestine. This inhibition was formerly thought to be solely due to a nervous reflex mechanism. It was found, however, that the motility of a transplanted gastric pouch was inhibited by ingested fat and that this was not due to the absorption of fat or fatty substance. This has been shown to be true also for the inhibition of gastric secretion caused by fat. Lim and his colleagues found that a crude preparation of cholecystokinin, when injected in large doses, would inhibit gastric secretion. This observation was then examined in detail, and it now appears that the inhibition of both gastric secretion and gastric motility caused by fat is due to a specific substance, which has been called enterogastrone. These observations have been confirmed.

Administration of Pepsin.—Pepsin as a therapeutic agent has passed through several periods of popularity since its discovery in 1835. In spite of this, practically no scientific evidence has been submitted showing that it is of real therapeutic value.

Theoretically, pepsin with adequate hydrochloric acid is indicated in achylia gastrica, particularly in those patients who complain of flatulent dyspepsia and diarrhea. Although such therapy is not infrequently employed in achylia gastrica, clinical reports are at variance in regard to the importance of the pepsin. Most of the recent reports indicate that hydrochloric acid alone is sufficient; however, others report that some patients do better after pepsin is added to the acid.

In the presence of gastric acidity there is some evidence indicating that, after the adequate administration of acid, a normal amount of pepsin may be secreted by the gastric glands. In such patients the addition of pepsin to the acid is superfluous. Whether the stomach of a patient manifesting anacidity will secrete adequate pepsin on the administration of acid can be determined only by fractional gastric analysis.

Recently several brief clinical reports have appeared indicating that the administration of desiccated hog's stomach (ventriculin) may be as effective as hydrochloric acid in relieving the dyspeptic symptoms and diarrhea in patients having achylia gastrica and anacidity.

Pepsin has been administered subcutaneously to patients having a "peptic" ulcer, and the claim has been made that pepsin plays a specific role. Both favorable and unfavorable reports on this therapy have been made. The rationale on which such therapy is based and the clinical reports now available are not sufficiently impressive to warrant a statement concerning the details of the therapy.

SUMMARY

(1) Certainly a good diet throughout life will aid in the prevention of anemia. Consideration of such matters as are mentioned later will do likewise. A careful study of near relatives of a pernicious anemia patient may reveal in one or more of them gastric achlorhydria with or without slight abnormality of the blood, although the individual considers himself well. In view of the familial incidence of pernicious anemia, the presence of achlorhydria in such a case may indicate a "latent" pernicious anemia. Liver therapy for that person may prevent, perhaps, the development of distinctive disease. The frequency of hypochromic anemia during the first year of life in babies born of anemic mothers may be minimized if such infants are given small doses of iron as a routine procedure.

(2) The anti-anemia factor consists of an intrinsic principle found in stomach tissue and an extrinsic principle derived from the food intake. Some investigators doubt that vitamin G, or the anti-pellagra vitamin, is to be identified with the extrinsic factor. The intrinsic principle produced in the stomach wall combines with the extrinsic food principle (as liver) to produce the anti-anemic factor, an excess of which is stored in the liver. Liver extract is believed to contain a combination of the intrinsic and extrinsic principles.

(3) The fraction of liver extract that contains the anti-pernicious anemia substance is rich in gastric secretagogic potency. This fraction stimulates gastric secretion on local application to the gastric and intestinal mucosa, thus acting as an hormone by the humoral route.

(4) The mucosa of the upper intestinal tract elaborates two hormones, namely: secretin and

cholecystokinin, and the inhibitory principle enterogastrone. The possibility that two other hormones are also elaborated has been suggested.

(5) Enterogastrone has long been known to inhibit gastric secretion and motility, particularly when the fat is in the intestine. This is not a reflex activity, but due to a specific substance which has been termed enterogastrone.

(6) Thus it would appear that much is to be learned in this field, in which marvelous discoveries have been made in the last decade. The gastro-enterologist may add much information by keeping accurate records of his tests, from time to time checking his findings against reports of others, and ultimately together with the experimenting physiologist, he may explain more and more of the mysteries of today.

(7) From inhibition to stimulation, with hormones as principle factors, intrinsic and extrinsic, we still have largely theories. Of many of the discoveries that benefit our patients we cannot explain the physiology. Certainly the beginning fault must lie among the triumvirate of the upper abdomen: liver, stomach and duodenum. One member's failure may be responsible, later involving the others, or all may become deficient at once. It is doubtful that the origin of anemia is purely from deficiency in diet. The possibilities of injury to one or all of these structures so affected by diseases from infancy on is obvious to all. The gastro-enterologist is acquainted with the many disturbances of digestion that afflict the American public. And so to test rigorously all secretions and excretions of our patients, the healing of the affected parts and supplying of deficiencies of these, the most important parts of the human anatomy, must be our aim.

CONCLUSIONS

(1) Liver therapy reactivates the hydrochloric acid in the stomach in the absence of trophic changes in the mucous membrane.

(2) Histamine is not always the best and only agent to differentiate between functional and permanent achylia. Liver substance should be tried in every case of achylia, even when the fractional analysis and histamine give a negative verdict.

(3) Systemic infection is a probable factor in achylia gastrica. It must be eradicated.

BIBLIOGRAPHY

1. Ivy, A. C.: Role of Hormones in Digestion. Physiol. Rev., **10**:282, April, 1930.
2. Cattell, McKeen; Wolff, H. G.; and Clark, Dean: Liberation of Adrenergic and Cholinergic Substances in the Submaxillary Gland. Amer. Jour. Physiol., **109**:375, Aug., 1934.
3. Romer, C.: Speicheldrusen and innere Sekretion. Mitt. a. d. Grenzgeb. d. Med. u. Chir., **40**:465, 1927.
   Rosenfeld, G.: Speicheldrusen Kohlehydratstoffweechsel. Klin. Wchnschr., **12**:711, May 6, 1933.
   Glaser, E.; and Bannet, L.: ibid, **12**:345, March 4, 1933.
4. Zimmerman, L. M.; and Soskin, Samuel: Effect of Ligation of Parotid Ducts on Carbohydrate Metabolism. Arch. Int. Med., **49**:409, March; 663, April, 1932.
5. Ivy; Klein, Eugene; and Arnheim, Ernest: Gastric Secretion: I. Transplanted Gastric Pouch. Arch. Surg., **25**:433, Sept., 1932.
   Klein, Eugene: II. Studies in a Transplanted Pouch Without Auerbach's Plexus. Ibid, **25**:442, Sept., 1932.
6. Klein; Arnheim; Klein, Kim; and Ivy, A. C.: On the Mode of Action of Secretagogues (Liver Extract) in Promoting Gastric Secretion. Amer. Jour. Physiol., **105**: 220, July, 1933.
7. Sacks, J.; Ivy, A. C.; Burgess, J. P.; and Vandolah, J. E.: Histamine as a Hormone for Gastric Secretion. Amer. Jour. Physiol., **101**:331, July, 1932.
8. Bloomfield, A. L.; and Polland, W. S.: Gastric Anacidity. New York: Macmillan Company, 1933.
9. Levin, A. L.: The Use of Liver Extract in Achlorhydria. Med. Jour. & Rec., Dec. 20, 1933.

DISCUSSION (*Abstract*)

Dr. E. Dice Lineberry, Birmingham, Ala.—Dr. Murry mentioned the use of ferric ammonium citrate and copper in the treatment of secondary anemia. The amount of copper necessary for the regeneration of blood is so small that adequate amounts are obtained in a diet of fresh fruits, green vegetables, milk, meat and eggs. Clinically, the administration of copper with inorganic iron has proven to be no more efficacious than inorganic iron alone.

The various inorganic irons are equally efficacious if given in adequate amounts. The two points to be considered when choosing the type of iron are the ease of administration and the cost to the patient. Fullerton (Edinburgh M. J., 41:99, Feb. 1934) has pointed out the daily dose and cost of the various irons commonly used:

Iron and ammonium citrate, daily dose, gr. 90; daily cost, 5 cents.

Blaud's pills, daily dose, gr. 45 to 60; daily cost, 6 to 8 cents.

Ferrous chloride, daily dose, gr. 5 to 7.5; daily cost, 6 to 9 cents.

Ferrous sulphate, daily dose, gr. 9; daily cost 2 cents.

Ferrous sulphate in bulk costs 30 to 35 cents wholesale. It is not only cheaper than the other iron preparations but the dose is so small that it rarely causes gastro-intestinal disturbances. For the past twelve months we have been giving five grains in capsules three times daily. The cost is so small that patients readily take it long enough to obtain the desired results.

PURPURA IN CHILDREN*

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Purpura, meaning a tendency to bleed into the skin and from mucous membranes, is a condition which occurs in a group of diseases. Like anemia, it is only a symptom; the underlying cause of either may present a very good or a very bad prognosis.

None of the numerous classifications of the purpuras is entirely satisfactory. No matter which of these one adopts or how conscientiously he attempts to defend his selection, he is apt to find many vulnerable points in his defense. We do not feel that we have anything to gain by attempting a discussion of the different groupings that have been suggested, but shall be content to follow Boyd[1] in simply dividing them into the secondary or symptomatic purpuras on the one hand and the so-called primary thrombocytopenic purpura on the other. In the first group, the condition is seen to accompany some definite disease or infectious process. It is more often associated with acute infections, the deficiency diseases, subacute bacterial endocarditis, pernicious or splenic anemia, leukemia, bone marrow tumors and chemical poisons. Henoch's purpura and Schönlein's purpura, which may be placed in this group, probably have an allergic basis. For our purpose here we need to go no further than this and shall immediately take up the discussion of the type with which we are now concerned, namely, thrombocytopenic purpura, or purpura hemorrhagica. A discussion of this condition by a pediatrician before a pediatric gathering is in order because it is relatively common in childhood.

It appears to be a definite disease entity and, as Boyd points out, it seems to be as closely connected with the thrombocytes as is pernicious anemia with the erythrocytes. It was first recognized and separated from the other purpuras by Werlhof[2] in 1735. He called it morbus maculosus hemorrhagicus. The next contribution to our knowledge of the condition was made by Hayem[3] when he discovered and described the blood platelets in 1877. He believed, however, that they were young erythrocytes. Four years later Bizzozero[4] corrected this idea and described them as distinct blood elements. About this time Brohm* reported two cases of purpura hemorrhagica in which the platelets were diminished in number. The same observation was repeated and emphasized two years later by Kraus.[5] Denys,[6] in 1887, observed the failure of the clot to retract normally. About 1910 to 1912 Duke,[7] by his investigations, established more definitely the relationship between the thrombocytopenia and hemorrhagic tendency. In 1914, Hess and Fish[8] called attention to the capillary resistance test as a means of distinguishing between purpura and hemophilia. Kaznelson[9] performed the first splenectomy on a case in 1916, thereby making the greatest contribution towards its successful treatment. Brill and Rosenthal[10] reported the first case of splenectomy in this country in 1923. Thus has gradually evolved our present knowledge, imperfect as it is, of this most interesting condition.

The etiology presents one of the unsolved problems of our day. We feel that there would be no advantage in our attempting to discuss the numerous causes that have been suggested. Nor is the exact relationship understood between the one outstanding clinical symptom, hemorrhage, and the constant pathological finding, thrombocytopenia. It was once held that the whole picture depended entirely upon an excessive rate of destruction of the thrombocytes by the reticulo-endothelial tissues. It was this idea that first suggested splenectomy to Kaznelson. However, investigators have concluded that this is not the whole explanation, but that some disturbance of the hemopoietic tissues causes defective platelets to be produced. Jedlicka and Altsschuller[11] found, at autopsy, evidence of defective megakaryocytes. Many believe with Leschke[12] that, whatever else may be present, there must be some defect in the capillaries which allows the blood to leak out. We shall leave the matter as it stands and agree with Boyd and others that the real truth lies somewhere between these various ideas.

The presence of purpura, like that of anemia, is easy to determine. It readily reveals itself through the spontaneous hemorrhagic spots in the skin, the bleeding from mucous membranes

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*Brohm, quoted by Leschke, E.; and Wittkower, E.: Ztschr. f. klin. med., **102**:—, 1881.

and the tendency to bruise easily. Nose bleed is very common. The type can be determined only by examination of the blood. Nor is the ordinary routine blood count sufficient. Thrombocytopenic purpura makes itself known by these definite findings: (1) the hemoglobin is not below normal except when reduced by loss of blood. (2) The erythrocyte count is normal unless it, too, is reduced through hemorrhage. (3) The total and differential leukocyte counts are usually unchanged. However, we not uncommonly find some degree of leukopenia in the acute cases, particularly in the earlier stages. Leukocytosis may later exist as a response to hemorrhage. (4) A reduced platelet count is the strongest diagnostic point. This is practically always below 100,000 and usually below 60,000. (5) The clotting time is apt to be normal, while the bleeding time is quite commonly prolonged well beyond the normal limit. (6) The clot which forms will not retract from the edges of a test tube. Another sign of less value is the so-called capillary resistance test. When a tourniquet is put around the upper arm sufficiently tight to cut off the venous circulation petechiae appear over the forearm in a very short while.

The clinical symptoms and course depend upon whether the condition is acute or chronic. If acute, the onset may be abrupt with loss of appetite, fever, malaise, irritability and general depression. The purpuric manifestations generally appear within 48 hours. Bleeding from the mucous membranes, especially from the nose, may be severe and persistent. In either type of case there may or may not be a moderate degree of splenic enlargement. The acute case presents three possibilities: (1) There may be complete recovery. (2) Death may result from exsanguination, intracranial hemorrhage or infection and toxemia. (3) It may pass over into the chronic type. Some writers, including Brill and Rosenthal, believe the chronic type to be more common in girls. Our experience tends to bear this out. Here the symptoms may be either continuous or intermittent with intervening periods of freedom from manifestations which last for months or even years. The platelets are apt to be abnormally low during the whole time. These chronic cases may present few clinical symptoms other than the purpuric spots, hemorrhages from the mucous membranes and the tendency to bruise from slight trauma. In all cases the final diagnosis is established by the blood examination.

Having made the diagnosis, one must decide what therapeutic measures are to be employed. This, necessarily, depends upon the type of case and the condition of the patient. The various agencies which have been advocated and used are: blood transfusion, calcium therapy, high protein diet, vitamin therapy, roentgen ray therapy, ultraviolet ray therapy, iron, antivenin, autolyzed liver, stomach mucosa, epinephrine, non-specific protein therapy, thromboplastin, moccasin venom and splenectomy. In our small series of cases each of these measures, except the moccasin venom, was employed in at least one case. In addition, one case which happened to have a gonococcus vaginitis had daily injections of theelin for eight days with no effect on the blood picture. Without attempting a detailed appraisal of these various therapeutic agencies we shall try to indicate the methods of treatment which seem to us to be worth while. The first step is to classify the case from the history and clinical course as either acute or chronic.

The acute case should be treated with the hope that it will either recover or pass over to the chronic type. These patients, when seen, are generally acutely ill, sometimes desperately so. They require the usual nursing care with attention to nutrition, fluid intake and elimination. Every effort must be made to stop loss of blood. Persistent epistaxis generally requires careful packing of the nares. The one agent upon which we must rely to tide them over the critical period is blood transfusion. On account of the effect the citrates have on the platelets, uncitrated blood is commonly recommended. But the technic of giving uncitrated blood to children is so difficult that it will generally be found to be impractical. Particularly is this true in view of the great number of transfusions that may be necessary. We have seen no evidence that the giving of blood has any curative value: it merely replaces what is lost from the vascular system and supplies enough blood elements for physiological function. Many writers advise small repeated transfusions. It is our observation that the amount and frequency must depend upon the patient's needs. The acute cases which are almost exsanguinated can be saved only by relatively large and frequent transfusions. One of our cases, a five-year-old boy who later had a successful splenectomy, was transfused 32 times in a period of about three months, receiving a total of about 8,000 c. c. of blood. The average case can be given

blood every two or three days, but in some of the more fulminating ones it may be necessary twice daily for a while. Calcium, iron and the vitamins seem to be without curative effect and are indicated in only such cases as suffer from a deficiency of these substances. Ultraviolet therapy may produce some general improvement in such patients as have been deprived of sunshine, but is apparently without specific effect. Our limited experience with such agencies as autolyzed liver, stomach mucosa, thromboplastin, epinephrine, non-specific protein therapy, high protein diets and roentgen ray therapy did not indicate that any of these was beneficial. Stockton and Franklin[18] and others found that injections of antivenin helped to control the bleeding. Our experience leads us to suggest that it be given intravenously in cases where hemorrhage is hard to control. Its administration by this route in one of our cases was followed shortly by a cessation of the hemorrhage and apparently complete recovery. Intramuscular injections in three others did not help.

Splenectomy is the one remedy which seems to be curative. It is indicated in the acute cases which have been carried over for a reasonable period of time by blood transfusions and in whom the clinical signs and blood picture do not indicate that recovery is taking place. It is clearly indicated in the chronic cases. Whether or not there is enlargement of the spleen makes no material difference. It should never be recommended until careful study of the blood establishes, beyond doubt, the diagnosis. The blood elements other than the platelets should be normal excepting what might be accounted for by response to hemorrhage. The reticulocyte count should indicate that the bone marrow is able to produce these cells at a normal rate. Aplastic anemia with purpura may be most difficult and it may require a period of very careful study to differentiate the two. A persistent and extreme leukopenia with a low reticulocyte count should be sufficient warning against operation. Leschke and Wittkower pointed out that prolonged bleeding from a puncture of the ear does not necessarily mean uncontrollable operative hemorrhage. Furthermore, surgeons have noticed, more than once, a cessation of any abnormal tendency to bleed almost as soon as the splenic vessels were ligated. Where the diagnosis has been carefully worked out the operation has nearly always been followed by satisfactory results. The bleeding tendency stops promptly or within a few hours and the platelet count reaches normal or higher in a short time.

In the light of our present knowledge we are not justified in saying the cure is complete and permanent. Some observers have noticed, after the initial rise in the platelet count, that it later dropped to the previous low level. However, this phenomenon has been accompanied by a return of the purpuric manifestations in only a few cases and then in a very mild form. Some investigators have felt that the return of symptoms might be due to the presence of accessory splenic tissue which, not being removed at operation, later developed compensatory increase in activity. The explanation which was advanced by Rosenthal[14] and others is quite reasonable. It is to the effect that, although a large portion of the reticulo-endothelial system has been removed by splenectomy, the remainder is probably stimulated to renewed thrombolytic action by the activating factor, whatever it may be. In spite of these factors of uncertainty regarding the completeness and permanency of the cure, the almost uniformly good results which have followed splenectomy justify the continued use of this procedure.

We here present brief summaries of thirteen cases admitted to the Crippled Children's Hospital in Oklahoma City during the past few years:

CASE REPORTS

Case 1.—A girl of 2½ years had had intermittent attacks of purpura for fourteen months. Three days before she was seen purpuric spots appeared over the body and the nose bled. She was not acutely ill. She was restless and irritable during the attacks, had frequency of urination and at times complained of abdominal pain. She had no fever and the spleen was not palpable.

Her hemoglobin was 80 per cent, erythrocytes 4,160,000, leukocytes 13,000, neutrophils 63 per cent, platelets 13,000, clotting time 6 minutes, and bleeding time 21 minutes.

She was under observation two weeks. She received large amounts of orange juice, cod liver oil and calcium, and heliotherapy daily. The gross hemorrhage stopped, but there was no change in the blood picture. The platelet count on discharge was 13,520.

This is the chronic, recurrent type and should have splenectomy.

Case 2.—This is a girl of 3 years. Petechiae appeared at two weeks of age. Purpuric spots developed later and had been present most of the time since, worse in summer. On admission spots were seen over the body and extremities. She was not acutely ill, and the spleen was not enlarged.

Hemoglobin was 85 per cent, erythrocytes 4,900,000, leukocytes 10,000, neutrophils 76 per cent, reticulo-

cytes 3.4 per cent, clotting time 8 minutes, and bleeding time 15 minutes. She was under observation eight days. She was given high caloric diet, cod liver oil and calcium. She was taken out of the hospital unimproved.

This is a chronic case, which should have splenectomy.

Case 3.—A boy of 5 years had had pneumonia three weeks before admission, followed by empyema. Purpura developed one week before. When seen he had left-sided empyema with purpuric spots over the entire body and extremities with bleeding from the tongue, gums, buccal membranes, right tonsil and nares.

His hemoglobin was 50 per cent, erythrocytes were 2,170,000, leukocytes 13,200, neutrophils 74 per cent, hardly enough platelets for a count, clotting time 6 minutes, and bleeding time 20 minutes.

He was given large doses of calcium, but died on the fourth day after admission. This was not a case of primary thrombocytopenic purpura and is reported merely to illustrate the secondary type due to infection.

Case 4.—A boy of 13 years had had symptoms for ten days, which consisted of generalized cramping in the abdomen and bleeding from the gums, which began on the fifth day. Later he developed purpuric spots over the entire body and passed tarry stools. When seen he was bleeding from the nose, was markedly prostrated, his pulse was rapid and thready, temperature 99.6° F., and spleen palpable.

Hemoglobin was 31 per cent, erythrocytes 1,910,000, leukocytes 8,600, neutrophils 70 per cent, small lymphocytes 20 per cent, large lymphocytes 10 per cent, reticulocytes 1.8 per cent, not enough platelets to count, clotting time 4 minutes, and bleeding time was 20 minutes plus.

He was given a transfusion of 400 c. c. of citrated blood with 150 c. c. normal saline and calcium gluconate intramuscularly. There was no lessening of hemorrhage. About 24 hours after admission he was given 10 c. c. of antivenin intravenously and this was repeated in 12 hours. All bleeding stopped about six hours following the first injection. He was under observation 23 days. He was given a total of 1,350 c. c. citrated blood, calcium therapy was continued and iron given. On discharge his blood picture was: hemoglobin 80 per cent, erythrocytes 5,130,000, clotting time 4 minutes, bleeding time 4 minutes, platelets 490,000, and he was clinically well.

This was an acute case. Apparent recovery followed transfusions. The antivenin seemed to help to control the bleeding.

Case 5.—A girl of 10 years had been ill for one week. Symptoms began with bleeding from the nose and gums with appearance of purpuric spots on the legs.

Her hemoglobin was 61 per cent, erythrocytes 2,680,000, leukocytes 5,400, neutrophils 70 per cent, reticulocytes 9 per cent, platelets 20,000, blood calcium 11.3 mg., clotting time 8 minutes, and bleeding time 20 minutes plus. She was under observation four weeks. She was given seven transfusions, each consisting of from 250 to 300 c. c. of citrated blood. Large amounts of calcium, orange juice, iron and ammonium citrate and dried stomach mucosa were given, and epenephrine subcutaneously. At the time of discharge there was almost complete disappearance of the purpuric spots. The blood picture was hemoglobin 84 per cent, erythrocytes 4,620,000, leukocytes 7,400, neutrophils 74 per cent, platelets 30,000, reticulocytes 2.3 per cent, clotting time 4 minutes, and bleeding time 12 minutes. Although there was an improvement in the general blood picture and the clinical condition which no doubt resulted from the transfusions and the diet, the platelet count did not appreciably improve. This looks like the beginning of a chronic type and the patient should have a splenectomy if there are further attacks of purpura.

Case 6.—A boy of 5 years had been ill for two months. He had nose bleed and purpuric spots over the body. There was shortness of breath and some cyanosis. His temperature was 101°. The spleen was enlarged 1½ inches below the costal margin.

Hemoglobin was 69 per cent, erythrocytes 3,850,000, leukocytes 4,200, neutrophils 70 per cent, reticulocytes 3.8 per cent, platelets 30,000, clotting time 7 minutes, and bleeding time 20 minutes.

During a period of about three months he was given 32 transfusions totaling about 8,000 c. c. of citrated blood. He had antivenin intramuscularly, autolyzed liver, large amounts of calcium, iron and haliver oil, high protein diet non-specific protein therapy and epinephrine. The bleeding continued and the blood picture changed little. Splenectomy was done. There was no further bleeding. The fourth day following operation the platelet count was 470,000, bleeding time 3 minutes, clotting time 4 minutes, and clot retraction was normal. Three weeks following operation he was discharged in good condition with a platelet count of 400,000.

This was an acute case which showed no tendency to recover. The blood picture was not affected by any of the many therapeutic measures until splenectomy was done.

Case 7.—A girl of 3 years had been acutely ill for seven weeks, with loss of appetite, swelling of the face, feet and abdomen with generalized purpuric spots and bleeding from the gums. The temperature was 101°. The liver and spleen were slightly enlarged.

Hemoglobin was 35 per cent, erythrocytes 1,870,000, leukocytes 3,900, neutrophils 64 per cent, reticulocytes 4.5 per cent, blood Wassermann negative, blood chemical tests normal, no malaria parasites, platelets 20,000, clotting time 6 minutes, and bleeding time 12 minutes plus.

She was given nine transfusions totaling 1,850 c. c. of citrated blood during a period of two weeks. She had haliver oil, calcium and epinephrine. The blood picture remained essentially the same. She developed pneumonia and died. Autopsy showed bilateral lobar pneumonia with pyothorax, enlarged liver and hyperplastic spleen.

This was an acute case which was not helped by treatment and which succumbed to an infection.

Case 8.—A boy of 5 years for two weeks had had nose bleed and purpuric spots over the body. He was acutely ill, with a temperature of 101°, pulse 120, and spleen moderately enlarged.

Hemoglobin was 20 per cent, erythrocytes 1,200,000, leukocytes 12,200, neutrophils 80 per cent, platelets 20,000, clotting time 6 minutes, and bleeding time 20 minutes plus.

During a period of nine days he was given 13 transfusions in amounts ranging from 150 to 450 c. c. of citrated blood, some intramuscular injections of smaller amounts of whole blood, high protein diet, large amounts of haliver oil, iron and calcium and 20 c. c. of thromboplastin intramuscularly. The day before death he was given 500 c. c. of 5 per cent glucose intravenously. Several hours before death he received 10 c. c. of antivenin intramuscularly. He died with signs of intracranial hemorrhage. No autopsy was done.

This was an acute case not helped by treatment.

Case 9.—A girl of 10 years had been ill for eight months with nose bleed and purpuric spots over her body. She was not acutely ill. The spleen was not palpable. The tonsils were septic.

Hemoglobin was 80 per cent, erythrocytes 4,030,000, leukocytes 13,550, neutrophils 69 per cent, eosinophils 1 per cent, monocytes 3 per cent, small lymphocytes 26 per cent, platelets 2,000, reticulocytes 1.5 per cent, clotting time 6 minutes, bleeding time 15 minutes, and clot retraction slight after two hours.

She was in the hospital 39 days. She had calcium, yeast, cod liver oil, iron, liver extract (intravenously), roentgen ray therapy to the spleen, and ultraviolet light therapy. There was no change in the blood picture. The last platelet count was 5,000.

This was a chronic case. Splenectomy was recommended, but her parents refused.

Case 10.—A girl of 11 years had been ill for seven years with frequent attacks of nose bleed, bleeding from the gums and purpuric spots, occasional vomiting of blood and passing of tarry stools. The tonsils were large, the superficial lymph nodes palpable, both liver and spleen moderately enlarged.

Her hemoglobin was 35 per cent, erythrocytes 1,470,000, leukocytes 5,900, neutrophils 78 per cent, small lymphocytes 22 per cent, platelets 61,600, reticulocytes 21 per cent, clotting time 4 minutes, bleeding time 9 minutes. There was no retraction of the clot after four hours. The blood Wassermann was negative, icterus index 8, van den Bergh, direct slight reaction, indirect too slight to read, and the fragility test was within normal limits.

She was given a high vitamin, high caloric diet with cod liver oil and iron, ultraviolet light therapy, and 13 small transfusions, ranging in amounts from 75 to 250 c. c. of citrated blood in a period of six weeks. Her general condition improved, but the platelet count dropped and was 4,000 preceding the operation. Splenectomy was done and the day following this the platelet count was 101,400. The child's condition was satisfactory, but three days after operation she developed pneumonia, from which she died. Autopsy was not permitted. The spleen showed chronic splenitis with numerous adhesions.

In this chronic case we feel that splenectomy would have been successful had the pneumonia not developed.

Case 11.—A girl of 2 years for 2½ months had had numerous petechial spots over the entire body and extremities, worse during the previous three days. She was not acutely ill and the spleen was not enlarged.

Hemoglobin was 80 per cent, erythrocytes 3,850,000, leukocytes 5,050, neutrophils 40 per cent, platelets 3,850, clotting time 2½ minutes, bleeding time 15 minutes, reticulocytes 7.2 per cent.

She was under observation eight weeks. Large doses of calcium and viosterol were given. Small amounts of whole blood were administered intramuscularly and two intramuscular injections of antivenin (5 c. c. each) were given, with ultraviolet light therapy. There was no change in the blood picture. The platelet count was 4,000 when she was discharged. She was readmitted to the hospital three months later with gonococcal vaginitis; there were no purpuric manifestations at this time. Hemoglobin was 85 per cent, erythrocytes 4,400,000, leukocytes 8,800, neutrophils 60 per cent, platelets 2,220, reticulocytes 1.4 per cent, clotting time 2 minutes, bleeding time 9 minutes, and the clot was nonretractile. She remained in the hospital over four months and had eight injections of theelin during the time. There was no change in the blood picture. The platelet count was 4,220 on discharge.

This is a chronic case which is apt to have future exacerbations. If so, splenectomy should be done.

Case 12.—A boy of 7 years had had conjunctival hemorrhage from the right eye, bleeding from the gums and purpuric spots over the entire body for the preceding five days. The spleen was not enlarged.

Hemoglobin was 78 per cent, erythrocytes 4,090,000, leukocytes 10,400, neutrophils 68 per cent, eosinophils 2 per cent, small lymphocytes 30 per cent, reticulocytes 2.2 per cent, clotting time 5 minutes, and bleeding time 15 minutes.

One transfusion was given of 400 c. c. of citrated blood, and he was under observation for ten days. Bleeding stopped. The blood picture when discharged was: hemoglobin 88 per cent, erythrocytes 4,390,000, leukocytes 9,700, neutrophils 54 per cent, and platelets 50,400.

This acute case may have followed some acute infection. The boy should be carefully watched and splenectomy done if symptoms recur and the characteristic blood picture persists.

Case 13.—A girl 13 years old for six years had had attacks of nose bleed, bleeding from the gums and purpuric spots over the entire body. There were long periods between attacks. When seen she was not acutely ill. There were numerous purpuric spots over the entire body. The spleen was moderately enlarged.

Hemoglobin was 85 per cent, erythrocytes 4,130,000, leukocytes 12,000, neutrophils 85 per cent, reticulocytes 1.1 per cent, platelets 16,520, clotting time 4½ minutes, and bleeding time 15 minutes.

She was under observation for one week. She received no treatment directed at the purpura except 20 c. c. of her own blood intramuscularly. The purpura improved, but the platelet count remained around 16,000. She left the hospital to return later for splenectomy. In this chronic case splenectomy should be successful.

The belief that the chronic form is more common in girls than in boys is borne out by this small series since all of our chronic cases, seven in number, were in girls. All of our male patients, five in number, had the acute type; only one girl presented this form. This would suggest further investigation of the possibility that the acute form may predominate in the male.

SUMMARY

Purpura, like anemia, is a symptom which is encountered in several different conditions. Thrombocytopenic purpura appears to be a primary blood dyscrasia which has a relation to the platelets similar to that which pernicious anemia has to the erythrocytes. It occurs in both the acute and chronic forms and its etiology is unknown. The diagnosis depends upon the finding of a low platelet count, normal clotting time, prolonged bleeding time and nonretractility of the clot. The acute form may terminate either by recovery, by death or by becoming chronic. The chronic form seems to be more common in females. The giving of repeated blood transfusions is a most valuable measure for prolonging life, but does not appear to be curative. The only effective remedy is splenectomy. This is indicated in the chronic cases and in the acute cases that have been given repeated blood transfusions for a reasonable length of time without evidence of recovery. It should be done only after a thorough study of the blood has established, beyond question, the diagnosis. Splenectomy cannot be said to effect a complete and permanent cure, as there may be some tendency for the symptoms to recur. However, the almost uniformly good results warrant a continuation of the procedure.

REFERENCES

1. Boyd, William: The Pathology of Internal Diseases. Philadelphia: Lea & Febiger, 1931.
2. Werlhof, Paul G.: Opera Medica. Collected by J. E. Wichman, 3 volumes. Hanover: 1775-1776.
3. Hayem, G.: Sur la nature et la signification des petits globules roughes du sang. Compt. rend. Acad. d. sc., **84**: 1239, 1877.
4. Bizzozero, J.: Uber einen neun Formbestandtheil des Blutes und dessen Rolle bei der Thrombose und der Blutgerinnung. Virchow's Archiv fur pathologische Anatomie, **90**:261, 1882.
5. Kraus, E.: Ueber Purpura. Inaugural Dissertation. Heidelberg: C. Winter, publisher, 1883.
6. Denys, J.: Etudes sur le coagulation du sang dans un cas de purpura avec diminution considerable des plaquettes. Cellule, **3**:445, 1887.
7. Duke, W. W.: The Pathogenesis of Purpura Hemorrhagica with Especial Reference to the Part Played by Blood Platelets. Arch. Int. Med., **10**:445, Jan., 1912.
8. Hess, Alfred F.; and Fish, Mildred: Infantile Scurvy: The Blood, the Blood Vessels and the Diet. Amer. Jour. Dis. Child., **8**:385, 1914.
9. Kaznelson, P.: Verschwinden der haemorrhagischen Diathese bei einen Falle von essentieller Thrombopenie (Frank) nach Milzexstirpation; Splenogene thrombolytische Purpura. Wien. klin. Wchnschr., **29**:1451, 1916.
10. Brill, N. E.; and Rosenthal, N.: Treatment by Splenectomy of Essential Thrombocytopenia (Purpura Hemorrhagica). Arch. Int. Med., **32**:939, Dec., 1923.
11. Jedlicka, V.; and Altschuller, G.: Chronic Essential Thrombopenia. Acta. med. Scandin., **64**:123, 1926.
12. Leschke, E.; and Wittkower, E.: Die Werlhopsche Blutifleckenkrankheit. Ztschr. f. klin. Med., **102**:649, 1926.
13. Stockton, Max R.; and Franklin, Geo. C. H.: Antivenin Therapeusis in Purpura. J.A.M.A., **96**:677, Feb. 28, 1931.
14. Rosenthal, Nathan: The Blood Picture in Purpura. Jour. Lab. & Clin. Med., **13**:303, Jan., 1928.

DISCUSSION (*Abstract*)

Dr. James H. Park, Jr., Houston, Tex.—Dr. Pounders has presented a clear picture of thrombocytopenic purpura. As he pointed out, splenectomy, performed upon subacute or chronic cases, usually is followed by prompt and striking improvement.

The operation, however, is hazardous in the acute stage, especially where serious hemorrhage has occurred, with the attending loss of platelets and decrease in blood volume. It is, therefore, desirable to build up the number of platelets and the blood volume and to lessen the bleeding time by means of transfusions of unaltered whole blood, vitamin therapy, calcium, heliotherapy, *et cetera*, before performing splenectomy. Even those measures may fail to produce the desired effect. It is then that irradiation of the spleen by means of x-ray should be considered. While the benefit accruing from such a procedure may be of only temporary value, it may serve to prepare the patient for splenectomy. It cannot be too strongly emphasized that splenectomy should be done only upon chosen cases where the diagnosis has been clearly established.

Dr. Jean V. Cooke, St. Louis, Mo.—Dr. Pounders has mentioned the lack of knowledge of the etiology of purpura, and especially thrombopenic purpura. One also has considerable difficulty in determining the best course to pursue in therapy of this condition. Remarkable variation may occur in the severity and course of thrombopenic purpura in children. There are, for example, those instances of fulminating course with very extensive hemorrhages that result in death in from 24 to 48 hours. These may follow such acute infections as scarlet fever or measles, and they occasionally occur without known preceding illness. There are also children who have an attack of typical thrombopenic purpura which, after transfusion, is followed by a return of the platelets to normal and no further manifestations of the dyscrasia. In certain instances such children may be observed in a second similar attack, from which they recover promptly. While there is no doubt that at the present time splenectomy seems to be the treatment of choice in chronic types of thrombopenic purpura observed over some weeks or months, it is sometimes difficult to decide in other instances whether splenectomy is to be advised. In certain cases with moderately severe acute or subacute thrombopenic purpura, one hesitates to delay the operation for fear the hemorrhages may become progressively more severe; yet, on the other hand, a number of such children have been observed to recover spontaneously, and to have no recurrence of the disease. We have had under observation, for example, a child with severe thrompopenic purpura with all the indications for splenectomy. Shortly before operation an increased fever prompted a

more careful blood examination, and although this had previously been negative for malarial parasites, large numbers were found. The purpura and thrombopenia disappeared promptly with antimalarial therapy. Occasionally dramatic disappearance of the bleeding and thrombocytopenia has occurred when splenectomy was carried out in a child obviously dying from severe and continued hemorrhage. In one such instance it was noted that the bleeding tendency apparently stopped abruptly during the operation. In the past ten years splenectomy has been carried out in the St. Louis Children's Hospital in only four instances of thrombopenic purpura. In all, the operation was apparently completely successful and no further thrombopenia was observed. One of these patients, upon whom the operation was done ten years ago, is now a prominent athlete.

Dr. F. M. Duffy, Enid, Okla.—May I ask Dr. Pounders whether a gingivitis existed in his cases?

About one year ago I saw a child who had all the clinical evidence of purpura hemorrhagica, including a normal clotting time, but no retraction time and prolonged bleeding time. A smear of this patient's gums showed numerous fusiform bacilli and spirilla of Vincent. She was given 0.5 c. c. of bismuth sodium tartrate at three-day intervals for three doses. In about ten days' time practically all clinical symptoms cleared up, including gingivitis, subcutaneous and submucous hemorrhage.

Dr. Pounders.—All these cases were given the usual complete physical examination, but no particular search was made for the organisms of Vincent. None was found. It might be well to follow up the suggestion and search for this condition in future cases.

Dr. Harvey F. Garrison, Jackson, Miss.—I have had splenectomies done in six cases of true thrombopenic purpura in children. Five of them made uneventful recoveries.

One case was lost. The blood picture of the patient was classical. Two factors probably contributed to our failure to cure the case. This child was fourteen months old and definitely allergic. He was subject to frequent attacks of vomiting and diarrhea, which, on many occasions, were very severe, and were followed by increased eczema and numerous purpuric spots varying in size from pinpoint to as large as the palm of your hand. Frequently there was a great deal of bleeding from the intestinal tract as well as the other mucous membranes.

These attacks, which came on frequently and were associated with loss of blood, made it difficult for us to build him up sufficiently to operate; but finally, it was thought that his condition would justify it, and we did a splenectomy. He apparently made a very fine recovery, and was doing well for about five months, at which time he began to have recurrent gastro-intestinal attacks, which were definitely allergic in character, and which were again followed by purpura and bleeding from the mucous membranes. He was given any number of blood transfusions, but it was impossible to build him up. After he died we did an autopsy and found an accessory spleen about the size of an ordinary lime.

There are two points that I especially wish to stress. First, as soon as a diagnosis of true thrombopenic purpura is established, if the patient's condition justifies it, a splenectomy should be done immediately. To attempt other methods of cure and delay longer is very dangerous. Splenectomy will cure the great majority of cases of true thrombopenic purpura.

Second, when operating, always look very carefully for an accessory spleen, as its presence has been known to prevent recovery in a number of cases.

The value of splenectomies in true thrombopenic purpuras cannot be too strongly emphasized.

EXPULSIVE CHOROIDAL HEMORRHAGE COMPLICATING CATARACT EXTRACTION*

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One of the most appalling experiences that may befall an ophthalmic surgeon is to stand helplessly by after a smooth section for the extraction of a cataractous lens and see the contents of the eye expelled by a deep intra-ocular hemorrage. The suggestive term "expulsive hemorrhage" for these unavoidable disastrous cases, in which the choroid and retina are torn loose and ruptured and coincident free bleeding forces out the contents of the eye, was proposed by A. Terson[1] in 1894. Fortunately the occurrence of postoperative choroidal hemorrhage is rare even in our present era when surgical treatment of cataract is so frequently practiced. The latest bibliography, compiled by Zeigler[2], includes only 214 cases. Ziegler gives credit to Baron de Wetzel as the first to observe a case of expulsive hemorrhage after cataract extraction. The case occurred in 1760, but was not reported until twenty-five years later when de Wetzel's son[3] published the details of the case. The relative frequency of this dreadful accident has not been definitely determined, though Würdeman[4] approximates its occurrence at three to a thousand operations. However, he suggests that

"As only the experienced surgeons are apt to report failures, the occurrence of postoperative accidents is probably greater than would appear from the viewpoint of statistics."

Expulsive choroidal hemorrhage is usually ushered in by a sudden and apparently severe pain in the eye and often with coincident trem-

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bling of the entire body resembling the ague of a chill. In some cases nausea and vomiting have been observed to come on coincidently with the bleeding. The hemorrhage occurs as a rule immediately after completion of the corneal section, though numerous case reports have been published in which it occurred just after delivery of the lens. Not infrequently the catastrophe occurs two or three days after operation and it has occurred as late as the tenth day. The gush of blood usually carries before it lens and vitreous and often the retina, choroid and ciliary processes and leaves a mass of clotted blood filling the eyeball and usually protruding from the gaping corneal wound. Some cases have been reported in which oozing from around the clot continued for several hours and some in which brief bleeding recurred at intervals for several days. In a few of the reported cases the bleeding took on alarming proportions. Although our discussion will be confined to hemorrhage complicating cataract extraction, it is known that spontaneous postoperative choroidal hemorrhage is not confined to this operation, that it may occur in any operation which necessitates opening of the eyeball.

The pathogenesis of expulsive postoperative choroidal hemorrhage is yet somewhat obscure. At present the opinion prevails that the true cases with massive bleeding are the result of rupture of choroidal vessels, although some observers favor the view that the bleeding is the result of a break in the posterior ciliary arteries. Bloom[5], who had the opportunity to make microscopic studies of four eyes removed soon after expulsive hemorrhage, demonstrated that the hemorrhage emanated in the choroidal veins and not the arteries. This observation has been verified by others. The blood collects between the sclera and choroid and as it increases in amount it finally ruptures the choroid and retina.

Many theories have been advanced regarding the cause of rupture of the intra-ocular blood vessels. Our present knowledge of the frequent occurrence of pathological changes in the blood vessels of those advanced in years and the coincident friability of the vessels would justify the assumption that weakened vessel walls enter largely into the etiology of postoperative spontaneous ocular bleeding. Hence the belief prevails that essential hypertension is a potent etiological factor in these cases. Equally plausible is the theory advocated by many that a preoperative increased intra-ocular tension suddenly reduced by emptying the anterior chamber exerts a negative pressure on the blood vessels of the choroid and thus results in their rupture. Tension may be so slightly elevated that it is scarcely noticeable, a condition frequently spoken of as a glaucomatous tendency, and yet be a factor in this serious class of cases. According to Melanowski[6] the glaucomatous state is not necessarily a constant one. He is of the opinion that it may be present intermittently, that a sudden transitory increased intra-ocular tension often occurs as a result of vasomotor disturbance coincident with emotional or nervous shock superinduced by the fear and worry of having to undergo surgical treatment. Many surgeons now agree that the emotional state is an important factor in the development of transient glaucoma. It would be fair to assume that local and constitutional factors may both play a part in the bleeding and that the reduced intra-ocular pressure coincident with decompression surgery favors a break in the weakened blood vessel wall. Some surgeons have attached etiological importance to the vascular relaxation following the employment of cocaine or epinephrine. Physical strain as it occurs during coughing, sneezing and vomiting paroxysms, and vigorous movements of the body must undoubtedly also be given a place among the possible causes of postoperative rupture of the choroid. It would hardly seem reasonable to assume that the so-called traumatic drag, the pull of the knife in making the section or the pressure induced in applying the fixation forcep could have any bearing on the etiology of these cases. Nor could faulty technic be blamed when it occurs in the hands of experienced operators. Hemophilia has also been placed in the category of possible causes.

Expulsive choroidal hemorrhage should not be confused with some of the less significant types of bleeding as of the iris, the ciliary body or sclera or with the blood diffusing into the anterior chamber from the conjunctiva, none of which are associated with extensive vitreous loss, extrusion of the retina and choroid or with a profuse flow of blood.

Little need be said of the prognosis as regards function in these cases, as it is self-evident that with such destructive bleeding the vision of the involved eye must be hopelessly destroyed. The flow of blood usually ceases after several hours and if asepsis is maintained the eyeball is preserved even though, after absorption of the clot, phthisis of the bulb prevails.

The management of these unfortunate cases resolves itself entirely into what can be done in a prophylactic way, for no effective treatment is known when once the profuse flow of blood has occurred. It has been suggested that the patient be placed in the upright position at the outset of the hemorrhage and pituitrin and epinephrin be administered hypodermically. To avoid graver consequences it is well to maintain asepsis, to apply pressure bandage and to quiet the disturbed patient with sedatives. Immediate removal of the disorganized globe has been advocated, but it occurs to me that enucleation should not be considered unless the hemorrhage becomes uncontrollable or in the event of subsequent panophthalmitis.

Because of the present belief that expulsive hemorrhage is induced either by a vascular or an ocular hypertension, these two conditions should be investigated in every case that is to be subjected to a cataract extraction. The patient with high arterial tension should be kept under the care of the internist for several weeks and in bed at the infirmary for two or three days prior to the operation. If such treatment fails to lower the arterial tension, blood letting has been recommended. In addition to this preparatory treatment Ziegler advocated that the patient be given ergot hypodermically, pituitrin (10 grains) or epinephrine (10 grains) two or three times on the day preceding the operation. It has been suggested by some surgeons that patients undergoing intra-ocular surgery should be given calcium for several days preceding the surgical treatment in order to insure rapid clotting of the blood. If there is reason to suspect glaucoma the patient should be hospitalized for several days prior to the operation and the tension taken at different hours of the day until the presence of glaucoma can be excluded. The tendency to hemorrhage would naturally be minimized by the use of purgatives a day or two before the operation, by rest in bed and by keeping the patient on a light diet. The suggestion of De Wecker[7] that a preliminary iridectomy, done a few weeks before the extraction, would lessen the liability of intra-ocular hemorrhage at the time of the extraction receives little consideration since de Schweinitz, Ziegler and others have observed cases of spontaneous hemorrhage at the time of the lens extraction in patients who had been subjected to the preliminary operation.

It would be difficult for you to form any conception of the sensation that comes over one during the first experience with a case of expulsive hemorrhage. This is especially true when it occurs on the operating table, with a sudden expulsion of the ocular contents, a deluge of blood and an irrevocable destruction of vision which follows immediately after completion of a smooth corneal section, while you stand aghast unable to render any assistance. It has been my misfortune to encounter four cases of post-operative choroidal hemorrhage of the expulsive type (in somewhat over 2,500 extractions), all occurring in my private practice.

Case 1.—The first of these occurred eighteen years ago in a man 63 years old, whose general health was apparently good, who presented himself with a bilateral mature senile cataract. As the case occurred before the clinical use of the sphygmomanometer, a study of the vascular system was not made. Urinalysis was negative. Intra-ocular tension was normal, McLean 28. Under local anesthesia (6 per cent cocaine) a smooth incision slightly in the cornea of the right eye had just been completed for the removal of the lens. Before any pressure had been exerted on the eyeball and with a perfectly quiet patient the lens came rapidly forward as though being pushed from behind. It was soon expelled spontaneously. A large quantity of vitreous and blood followed and the choroid and retina were extruded. The patient complained of pain, though not severely; however, he seemed to sense that something unlooked for had occurred and became very nervous and shaky. Morphine (¼ grain) was administered hypodermically, the protruding vitreous and membranes were cut off, pressure bandage was applied, and the patient put to bed. At the first dressing, two days after the operation, the eyeball seemed filled with clotted blood, and a mass of blood occupied the space between the gaping lips of the wound. Gradual resorption of the clot took place, leaving a shrunken eyeball. The purpose of the operation, restoration of vision, was a total failure.

Case 2.—A woman 48 years old applied for the removal of a complicated cataract from her left eye for cosmetic reasons in April, 1930. The eye was divergent, the lens opaque. There was no light perception. Intra-ocular tension was high (McLean 50). The right eye was normal, vision 20/20. Blood pressure was 135/80. Physical and laboratory examinations indicated perfect general health. The patient was kept under pilocarpine and eserine instillations and the internal administration of iodine for two weeks, which reduced intra ocular tension to 32. As the operation was to be done for cosmetic purposes, a simple extracapsular extraction was contemplated. The patient had been given 3 grains of sodium iso-amylethyl barbiturate an hour before operation. Cocaine was used as local anesthetic. Immediately after the completion of the section, which extended slightly into the cornea, the lens came forward and in a few seconds was expelled. Vitreous followed, also quite a gush of blood. A pressure bandage was applied. Although the patient had been perfectly quiet during the operation, she complained of pain with the occurrence of the hemorrhage and was therefore given ¼ grain morphia and put to bed. Some shrinkage of the eye followed. However, from the viewpoint of the

patient, who was expecting only a cosmetic result, the operation was a success, as she was able to wear a shell over the phthisical eye with considerable improvement in her appearance.

Case 3.—A man 73 years old consulted us in May, 1933, regarding failing vision of both eyes. His right eye had an immature cataract, with a wide pupil. Intra-ocular tension was 45 (McLean). There was no light perception. The left eye had an opaque lens almost mature, vision with correction 20/70. The visual field was slightly constricted for form and color. The pupillary response to light and projection was fairly rapid. Tension was 40. His cardiovascular system had been examined by Dr. Morris M. Weiss, who reported a generalized arteriosclerosis. Urinalysis was negative. Blood pressure was 140/80. Under pilocarpine and eserine instillations tension in both eyes was reduced in ten days to 32. A large peripheric iridectomy was then done on the left eye and four days later on the right one. When the patient returned six months later, having used miotic treatment regularly, he had a fairly deep chamber in the left eye, a well reacting pupil, a more advanced cataract and vision reduced to 20/200. Intra-ocular tension was 28, blood pressure 140/70. The patient was kept in bed at the infirmary for twenty-four hours. He was given the usual preliminary care, which included 3 grains of sodium iso-amylethyl barbiturate an hour before operation, and the eye was prepared for intracapsular removal of the left lens; cocaine 6 per cent instillation; novocaine injections of the lids and retrobulbar area. Operation done by my associate, Dr. C. Dwight Townes, included superior rectus bridle, preparation of conjunctival flap, and large smooth section. As an attempt was made to dislocate the lower edge of the lens with capsule forceps, the anterior capsule ruptured and apparently was completely withdrawn. The lens was readily removed without compressing the ball. As no remnants of cortex were visible, the anterior chamber was not irrigated and the eye not subjected to further manipulation. At the first dressing, three days after operation, the anterior chamber had reformed, the pupil was open and black and only one or two small remnants of lens matter were visible in the anterior chamber. There was no sign of hemorrhage. With casual test he was able to count fingers and could distinguish objects about the room. Twenty-four hours later (four days after extraction) the patient had a sudden severe pain in the eye which had been operated upon, and when the nurse answered his call she found his dressing blood-soaked. The nurse reported continuance of pain and considerable excitability until she administered ¼ grain morphia hypodermically. Two hours after the accident the case was seen by Dr. Townes, who found a large blood clot protruding from the wound, the conjunctiva having torn from the suture. This case also terminated disastrously, phthisis bulbi ensuing with total loss of vision.

Case 4.—A woman, 85 years old, consulted us on May 31, 1935, on account of failing vision. Examination revealed senile cataract developed almost to maturity in both eyes. Vision in each eye was 20/200. There was rapid pupillary response to light and definite projection. Intra-ocular tension on the right was 32 (McLean), left 30. Physical and laboratory examinations were negative. Her blood pressure was 170/85. On July 4, 1935, the patient was prepared for operation as in the previous case. With the eye fixed by means of a superior rectus suture and a small conjunctival flap prepared, extracapsular extraction with iridectomy was done. The lens was readily removed. There was no further manipulation of the eye, no irrigation, and the conjunctival suture was tied. Four hours after the operation the nurse was called and found that the patient had just suffered a sudden and sever pain in the eye that was operated upon. She was in a hard chill and was vomiting. The eye dressing was saturated with blood. The patient was so nervous that it could not be determined whether the vomiting preceded the eye symptoms or whether it followed the ocular pain and hemorrhage. Morphine (¼ grain) was ordered by 'phone. When seen an hour later she was quiet. Removal of the dressing revealed a very large clot in the gaping wound. The conjunctival flap was disrupted and the clot was large enough to protrude between the eyelids. This case terminated as did the others in phthisis bulbi and total loss of vision.

CONCLUSION

Based upon my limited number of cases and the experience of others the following conclusions seem justifiable:

Expulsive hemorrhage following uncomplicated cataract extraction is a rare occurrence, though it seems to be gaining in frequency.

The condition is recognizable by the sudden and profuse flow of blood, forcing out the contents of the eyeball and filling the globe with clotted blood.

Postoperative laboratory findings would indicate that the hemorrhage results from ruptured choroidal veins.

We can look upon vascular degeneration, systemic hypertension and the glaucomatous state of the eye as the predisposing causes of expulsive hemorrhage, and the sudden release of intra-ocular tension coincident with decompression of the eye as the exciting cause.

The hemorrhage nearly always destroys vision.

No treatment applied at the time of the hemorrhage is of much avail. Treatment must consist of prophylactic measures, chief among which is careful attention to the vascular and the intra-ocular tension.

The probability of emotional shock must be reduced to a minimum by preoperative rest in bed in cases where this seems indicated and by the administration of sedatives before the operation.

Procaine hydrochloride injections of the lids and the retrobulbar structures at the time of the operation should be practiced to reduce intra-ocular pressure and manipulation of the

eye during operation should be reduced to a minimum.

BIBLIOGRAPHY

1. Terson, A.: Arch. Ophth., **17**:110.
2. Ziegler: Contributions to Ophthalmic Science, ——:—— (March) 1926.
3. de Wetzel: Traite de la Cataracts, Paris, p. 125, 1786.
4. Wurdman: Amer. Jour. Ophth., p. 427, 1926.
5. Bloom: Arch. Ophth., **46**:184.
6. Melanowski: Kliniki Oczne, **2**:205, 1933.
7. De Wecker: Arch. d'Ophth., **12**:662, 1892.

DISCUSSION (*Abstract*)

Dr. H. G. Reynolds, Paducah, Ky.—I am one of those lucky individuals in that over a period of thirty years with the average practice, I have never had this unfortunate accident in cataract extraction. Yet, I am reminded of the experience of the late Dr. Charles Beard, of Chicago, who had reported twelve hundred cataract operations, stated that he had never had an expulsive hemorrhage, to be followed in the next few operations with two of these complications, with the loss of both eyes and I think both were iridectomies.

Elsnig gave a full and enlightening report of his work in Prague during twenty-five years from 1907 to 1916. In one thousand cases there were six expulsive hemorrhages; in the next thousand, three expulsive hemorrhages. In the next thousand, two; the next thousand, two; and in the next twelve hundred which ended in 1930, no expulsive hemorrhages.

Can we agree with him that this result was due to precautionary preparation which was introduced in this clinic, such as special preparation of the patient with high blood pressure, venipuncture before operation if necessary, medication to overcome any inclination to bleed, akinesia at operation and retrobulbar injections of procain-epinephrine which reduces the intra-ocular pressure for a longer time?

The essayist took all these precautions in his four cases, the blood pressure was normal, the intra-ocular tension was about normal and yet the accident occurred and can be accounted for almost certainly, by what Elsnig refers to as brittle blood vessels.

N. Blatt's abstract (1929) on the clinic at Jassy reported 989 extractions of cataract in which there were eight cases of expulsive hemorrhage. In twenty-three per cent of all these cases, there was evidence of hypertension in the arteries, but expulsive hemorrhage did not occur in any of them. He says in conclusion that systemic hypertension cannot be considered as the cause of expulsive hemorrhage, nor can the latter be avoided if an attempt is made to lower the hypertension before operation.

Any addition to our armamentarium that assists us in combating this complication in cataract extraction is welcome. One not mentioned by the essayist, with which I have had no experience, but advocated by Duke Elder, is worthy of consideration. It consists of "injection of one c. c. per kilogram of body weight of a 30 per cent solution of sodium chloride intravenously. Inject slowly and evenly over a period of ten minutes. Do not give the patient any water. The lowering of the intra-ocular pressure, which is marked, lasts a day or two." Woodruff tried this experiment in six cases in the Illinois Eye and Ear Infirmary and stated that the reduction in ocular tension in these cases was constant and lasted at least twenty-four hours.

Quoting Lambert and Wolfe, he concludes that it will produce a drop in ocular tension, lasting only two hours in normal eyes, but twenty-four hours in glaucomatous eyes. It has no great use in tension controlled by miotics, but has its greatest use in eyes not controlled by miotics, therefore it is of great use in preventing hemorrhage and loss of vitreous.

The conclusions of the essayist are sound, but we shall continue to have expulsive hemorrhages in spite of all of our preoperative care.

Dr. W. R. Buffington, New Orleans, La.—My experience with this surgical catastrophe has been limited. I shall confine my discussion to a distinct postoperative complication; namely, spontaneous hemorrhage from the anterior segment of the eye, subsequent to cataract extraction or iridectomy. This complication comes on quite spontaneously after the 24-hour period following uncomplicated cataract extraction.

Derrick T. Vail, in a careful review of this subject in 1933, concludes that it occurs with greater frequency from three to five days after operation. Wheeler says it may happen at any time up to the twenty-eighth day. Worth is more precise, giving the time at the one hundred twentieth hour after the operation. There may be two or more hemorrhages. In a large series of cases from different operators, the complication averages 7.6 per cent (Vail). This postoperative complication has occurred six times in five patients: Four times in 204 private cataract extractions and twice in 49 private preliminary iridectomies which I have done in one institution since 1931. The record shows that three were in the fifth decade of life and two in the sixth.

In none of my cases is there a history of trauma after operation. In all except one the hemorrhages occurred at night, causing severe pain and awakening the patient. In none of the cases were there any immediate operative complications. At the time of the hemorrhages very mild postoperative reaction was present. In two cases, two hemorrhages occurred; in all cases the hemorrhage was sufficient to fill the anterior chamber, reopen the incision, pass out and partially saturate the small gauze dressing next to the eye. The eyes operated upon in all instances were protected by Ring masks. In each case the hemorrhage was responsible for a prolonged convalescence, due chiefly to a severe iridocyclitis, a complication secondary to the hemorrhage. In none of the five patients was increased intra-ocular tension present before or after the operation. Final visual results in four cases were 20/30 or better; the fifth case is convalescing. This indicates good prognoses.

In Case 1, there was a hemorrhage of the nature described after the iridectomy and the second hemorrhage followed the cataract extraction some months later. In Case 4, recurrent hemorrhage took place following the iridectomy. Three injections of whole blood were given in this case. About fifteen hours before the extraction of a cataract a 250 c. c. blood transfusion was given. There was not the slightest evidence of hemorrhage subsequent to the cataract extraction. This patient was a mild controlled diabetic. In Case 2 following cataract extraction the hemorrhages occurred on the fifth and on the seventh days, in spite of the use of calcium and coagulum. After the second hemorrhage, a 200 c. c. blood transfusion was given. There was no recurrence.

Preliminary iridectomies were done in three of these

cases. In one case there was a combined extraction. The hemorrhages occurred as follows: Case 1, at the end of four days; Cases 2, 3 and 4, at the end of five and a half days; and Case 5, at the end of four days, making an average of 4.9 days in each case, or a total of 118 hours.

I am sorry that I did not get Dr. Pfingst's paper early enough to review the data of my clinic cases at Charity Hospital. I can state, however, that among my clinic cases this complication has in some instances resulted in serious damage to the effected eyes.

The treatment of this condition is most important, but it cannot be taken up in this discussion.

A TRACHEOBRONCHIAL SUCTION TUBE*

By W. B. McWhorter, M.D., F.A.C.S.
Anderson, South Carolina

The accompanying picture shows an instrument (different from any other on the market) which I have found very useful for the removal of secretions from the larynx, trachea and upper bronchi. It can be inserted quickly and easily by any physician having knowledge of the anat-

omy. In laryngeal diphtheria and in cases of tracheobronchitis due to foreign bodies, thick secretions form which often cause suffocation unless they are removed. I have never used it in pneumonia, but see no reason why it cannot be used with benefit in appropriate cases. After insertion of the tube into the larynx or upper trachea suction may be applied directly to the tube. If the physician desires, a soft rubber catheter can be inserted into the tube and passed down into the trachea. Suction applied to the catheter will evacuate the trachea and upper bronchi. The instrument can also be used as a life-saving tube until intubation or tracheotomy can be performed. It is much more easily inserted than the ordinary intubation tube or the bronchoscope. The instrument is made in two sizes. The smaller will admit a size 12 catheter and is for children of three or younger. The larger will admit a size 14 catheter and is used in children over three.

*Received for publication December 11, 1935.

FRACTURE OF THE SHAFT OF THE FEMUR*

By Henry G. Hill, M.D.
Memphis, Tennessee

In November, 1927, with Dr. Jarrell Penn, of Knoxville, who at that time was associated with me, I reported in the *Journal of the Tennessee State Medical Association* results obtained and methods employed in the treatment of 92 cases of fracture of the shaft of the femur. Since that time I have treated a considerable number of cases, and have followed the treatment advocated then with results that compare favorably with any that I have seen reported. My chief reason for selecting this subject is the confusion and divergence of opinion regarding the treatment of these injuries that have been expressed in the literature during the past few years.

Mr. W. J. Eastwood,[1] in the *British Medical Journal*, said:

"The methods of treating fractures of the shaft of the femur become increasingly numerous as each fresh number of the medical journals is published. Much ingenuity is displayed in devising these new methods, which are almost invariably modifications of the older methods, and these modifications are usually complications. Hugh Owen Thomas, in 1870, described a simple method of treating this fracture by means of a splint devised by him and called the Thomas bed knee-splint.

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Twenty-Ninth Annual Meeting, St. Louis, Missouri, November 19-22, 1935.

This splint is used with fixed extensions, and the method in all its simplicity has been used in Liverpool and by the Liverpool school since that date. It is easy to apply and, if used correctly, gives very satisfactory results, but two things are essential: (1) a thorough knowledge of the Thomas splint; (2) very careful attention. It is probably because of the lack of knowledge of these essential features that this method in some hands has given unsatisfactoy results.

"I have reviewed in this paper every fracture of the shaft of the femur, without exception, which was admitted into Alder Hey Hospital, Liverpool, and into Wigan Infirmary during the year 1931. The majority were easy to treat, a few caused some anxiety, and one or two were distinctly difficult; but all were treated on a Thomas splint with fixed extensions. Detailed notes of these cases, the ages of which range from 2 days to 67 years, are given at the end of this paper.

"Of the sixty-one cases reviewed, ten had shortening of some degree, twenty-one had full length, and thirty had up to an inch of lengthening. Of the ten who had shortening, two were discharged from the hospital, one, one-quarter of an inch too long and the other with half an inch lengthening. Both discarded their calipers on arriving home, because their mothers thought they walked better without them. Of the other eight, the shortening in five of them was a quarter of an inch, in two it was half an inch, and in one, which was very bad, it was three quarters of an inch. All these eight patients were between the ages of 6 and 19 years, and no excuse other than lack of constant attention can be offered for these poor results."

Quoting from an article by Hendon[2], of Louisville, on the same subject:

"The treatment of this injury always has been a more complicated and difficult problem than the treatment of fractures of any other of the long bones.

"I shall not deal with the methods that are in vogue and well-known to surgeons, but will confine myself to a description of a plan which I have evolved and employed in 33 cases. My series include all the various types of fracture that occur in civil practice, namely: simple, compound, comminuted, complicated, transverse, oblique, spiral, gunshot, and infected fractures and nonunion, as well as vicious union. I have in most instances been able to reduce the period of disability to at least one-half the time required by the prevailing methods; while the comfort of the patients has been immeasurably enhanced and the results have closely approached the ideal. My plan does not entirely depend upon the cardinal principles involved in the treatment of fractures, such as splinting, suspension and skeletal traction.

"As you no doubt have already surmised, the plan contemplates the use of a device that is made of beef bone which I have dignified by the name of 'key.' I call it a key because there are certain locking principles involved in its use that make it more than a pin or peg, but under no circumstances should it be considered a graft, as its growth is neither expected nor desired."

A very detailed description of the apparatus and method of treating fractures of the femoral shaft appeared in the July, 1935, issue of the *Journal of Bone and Joint Surgery*.[3] The author advocates the use of his special skeletal traction and suspension in all types and feels that he has solved the mechanical difficulties incident to treatment.

One only has to review the literature to realize how impractical many of the methods in vogue are; and a study of results obtained in various hospitals throughout the country suffices to warrant the belief that there is room for improvement in the treatment.

Restoration of function is our goal. This we can expect in a large percentage of cases, provided we stick to the fundamental principles governing the treatment of all fractures, regardless of whether it be a compound, comminuted fracture of the femur or a simple transverse one in the distal phalanx of the little finger. Permanent, partial loss of function, shortening and deformity should be rare exceptions, not the result expected. Decide in each case the problem presented and select apparatus accordingly. The value of any apparatus is of less importance than the skill with which it is used. Roentgen ray examinations should be made as early as possible; fluoroscopic control is worth while, if intelligently carried out in appropriate cases.

There is no standardized method of treating fractures of the shaft of the femur; there is no standardized apparatus. Each case differs in some respects from the other. The injury is sustained in a different manner, under different circumstances, and the degree of severity varies. Still the essential cardinal principles of treatment are always the same, namely: reduction and immobilization. Reduction of the fracture as early as possible should be as complete as the individual case requires. Further attempts at reduction should be made as soon as the need is recognized. The fragments should be immobilized until union has taken place, the surgeon being the sole judge as to just how the fracture is to be reduced and splinted.

Primary treatment or first aid is very important. If a patient is seen on the roadside in a state of severe shock, with a compound fracture of the thigh, what should be done? Cleanse the wound, attempt to reduce the fracture and splint the limb. "Splint 'em where they lie," administer indicated general treatment, then transport them. The thought I wish to convey is: never neglect the fracture on account of the general condition of the patient. Do not allow a fractured extremity to dangle while transport-

ing. Shock and pain are mitigated by efficient splinting.

Secondary treatment consists of study of the individual case and selection of a method of treatment that will restore function within the shortest period of time.

Compound fractures present two problems: first, the prevention of infection developing within the wound; second, the reduction and splinting of the fragments. For the purpose of discussion, it is convenient to consider these separately; however, actually both should be carried out simultaneously. If the wound is successfully treated and infection fails to develop, the injury becomes a simple fracture and the problem of splinting is greatly simplified. If attention is directed to the soft tissue injury only in an effort to prevent or suppress infection and the fracture is neglected, results are almost uniformly disastrous. It is conclusive that imperfect immobilization of fragments in a vicious position favors the development and continuation of wound infection. Edema lowers the resistance of the soft tissues and bone offers but slight resistance to infection. For this reason, septic processes easily invade the bone once they develop in the wound. Ostoemyelitis is a serious complication and may continue for years if once established. Non-union, shortening, angulation, or muscular atrophy, with loss of function, can be expected if a chronic osteomyelitis occurs.

Methods Followed in Treatment.—Approximately 7 per cent of my cases occurred in children under 5 years of age. These were treated with overhead skin traction; results are uniformly good. About 60 per cent of my cases are treated by immediate reduction and application of plaster of paris cast. In the transverse and slightly oblique cases, the fracture usually can be reduced and the fragments locked or engaged in such a way that displacement will not recur, if the reduction is carried out on a fracture table, the cast applied and allowed to set before the patient is moved. Care should be taken not to injure the knee joint. Joint stiffness and atrophy of the articular cartilage, as a rule, is the result of injury to the periarticular structures. The late Sir Robert Jones positively stated that immobilization of a joint in the normal physiological position would not produce permanent stiffness. Ill-fitting casts, improperly applied, with an unequal distribution of pressure, are responsible for the opinion among certain surgeons that plaster of paris does not make a suitable splint for external fixation. When the fragments cannot be manipulated into a satisfactory position and locked, as is the case in certain oblique, spiral and comminuted fractures, as well as in a limited number of transverse, some other method of treatment should be undertaken. An overlapping of fragments, shown on an accurately made x-ray film or fluoroscopic screen, means that there will be permanent deformity if they are allowed to remain. One must not expect any form of external splinting to prevent deformity when the fracture has not been reduced.

Caliper Reduction.—Supracondylar and epiphyseal fractures with wide separation of fragments, together with a limited number of the transverse and oblique types, are reduced with the aid of calipers. When the fragments are proven to be in proper alignment, a cast is applied, the caliper being moulded into the plaster. I have used this method of treatment in about 12 per cent of my cases. The calipers may be removed within 24 hours or allowed to remain for a week or ten days, depending upon the stability of the fragments after reduction. I know of no other surgeon who follows this exact procedure, which, when indicated, has some advantages over the methods of skeletal traction, commonly advocated.

Skeletal Traction. — Comminuted, multiple, certain oblique, spiral and compound fractures are best treated by some form of skeletal traction. Pins, wire and calipers have all been used. I prefer the calipers in most cases. The method is very efficient. I have employed skeletal traction in conjunction with the Thomas splint and overhead frame in approximately 11 per cent of my cases. Results have been excellent, the chief disadvantage being the necessity of the patient's remaining in the hospital for a prolonged period. The position of the fragments should be checked frequently with the x-ray in order to determine the amount of weight necessary in guarding against over-extension. It is essential to give the patient close attention. He should be seen twice daily. Close supervision is quite as important as a proper installation of appliance. The cost of treatment exceeds

that of other methods. It is hardly practical to advocate skeletal traction in the treatment of all cases, when the simpler methods meet all requirements in many instances.

Open Method.—In 10 per cent of the fractures of the femur that I have treated, open reduction was decided upon. It is generally agreed that this is the method of last resort. There are, however, some cases, for example, delayed union with vicious position of fragments, nonunion or vicious union and displaced fragments with interposed soft tissue, which are best treated by the open method. Infection, of course, would be a tragedy and should occur so rarely that it can be eliminated as an objection to the open method. Needless to say, open reduction should be undertaken only in a well equipped hospital by a surgeon familiar with the hazards of bone surgery. When it becomes necessary to stimulate osteogenesis or fix the fragments with an internal splint, the autogenous bone graft has the weight of experience in its favor. The percentage of failures following the use of foreign materials of all descriptions forestalls any discussion of this point.

In compound fractures, debridement operation should be done diligently, always considering in advance the ultimate functional results.

CONCLUSIONS

(1) The underlying principles governing treatment of fractures in general should be carried out in treating fractures of the femoral shaft.

(2) There is no single method of treatment suitable for all types of fractures of the femur.

(3) There is no logical reason to allow the fragments to unite in an overlapped position. To do so invariably causes prolonged and partial permanent disability.

(4) Present day literature is very confusing. Enthusiasm should not replace sound surgical judgment.

REFERENCES

1. Eastwood, W. J.: Fractures of Shaft of Femur. Brit. Med. Jour. (January-June), 1933.
2. Hendon, G. A.: Fractures of Shaft of the Femur. Amer. Jour Surg., **20**:1933.
3. Cordorniu, Antonio H-Ros: A Synergical Splint with Traction for Femoral Fractures. Jour. Bone and Joint Surg. (July), 1935.

PYLORIC STRICTURE FOLLOWING THE INGESTION OF MURIATIC ACID*

By Jay M. Arena, M.D.
Durham, North Carolina

A white boy, aged 2 years, entered Duke Hospital on March 25, 1935, because of vomiting of two weeks' duration. The family and past histories were unessential except that he was one of identical twins and because of inadequate vitamins and poor diet had developed rickets. On February 25, 1935, he swallowed by accident about a tablespoonful of muriatic acid (concentrated hydrochloric acid) and was taken to his physician, who lavaged the stomach about 30 minutes later. He vomited black-greenish material several times afterwards. However, he seemingly did well for the following two weeks. There was no vomiting and his appetite was normal. On March 8, 1935, he began to have projectile vomiting, often vomiting immediately after meals. At times the parents noticed that the vomitus contained material ingested several hours previously. His stools became less frequent and finally there was obstipation. He lost about ten pounds of weight and when admitted to Duke Hospital he was greatly malnourished and dehydrated. He had obvious rickets. The tonsils were enlarged, but not injected. The heart and lungs were normal. The abdomen on inspection showed a full rounded mass in the upper quadrant. At this time he had projectile vomiting and the vomitus contained numerous undigested peaches which had been eaten six hours previously. The abdomen then became scaphoid and the mass disappeared. Rectal examination was negative. The accessory laboratory findings were of no significance.

Immediately after the patient was admitted, he was given parenteral fluids. He took liquids and solids greedily, but was unable to retain either. Barium studies of the esophagus showed no evidence of any stricture or cardiospasm. After the stomach was fairly well filled, rather marked and exaggerated peristalsis was seen. The pyloric channel could be poorly visualized and was markedly stenosed and elongated, and very little barium passed through it during the observations. An esophagoscope was passed and a moderate stricture of the cardiac end of the esophagus was found. On several occasions following projectile vomiting a small mass about 1 cm. in diameter could be palpated at the pylorus. After he had been "built up" with parenteral fluids and blood transfusion, an exploratory laparotomy was performed on April 4, 1935, and a somewhat indurated mass in the region of the pylorus was found. The duodenum was not involved. The mass was not as large as is found with congenital pyloric stenosis, but it involved the pyloric end of the stomach for a distance of about 6 cm. The serosa and muscularis were incised and the other fibers were separated by blunt dissection down to the submucosa. This region, however, did not herniate, but was markedly thickened and scarred. Because of the condition of the pylorus a Finney pyloroplasty was then done.

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*From the Department of Pediatrics, Duke University School of Medicine, and Duke Hospital.

The postoperative course was uneventful. The patient was slowly started on solid food and had no difficulty. He was discharged in good condition on the twenty-seventh day after the operation. The esophageal stricture was so mild that monthly dilatations were sufficient to maintain an easily patent esophageal passage.

COMMENT

Lye is the most common corrosive taken by children and consequently the esophageal lesions are well stressed in the pediatric literature. However, the ingestion of lye does occasionally produce gastric lesions which may complicate the picture. On the other hand, the ingestion of acid seems to have its maximum effect on the pylorus, leading to pyloric obstruction, which may easily be confused with late pyloric obstruction due to other factors.

As early as 1902, Quenu and Petit[1] were able to collect eighty-four references from the European literature on the subject of gastric sequelae following ingestion of corrosive liquids. Since then there have been many additional reports, but only recently has the subject been discussed in the English literature.

Boikan and Singer[2] have reported five cases, in adults, who accidentally or for suicidal purposes ingested corrosive liquids. All of these, within variable periods, had symptoms of obstructive vomiting, loss of weight, and roentgen evidence of obstruction in the stomach alone or in combination with the esophagus. Vinson and Hartman[3] reported a case in which an esophageal stricture was effectively treated by dilatation, but was followed six months later by pyloric stenosis which eventually led to death. McLanahan[4] reported a case of pyloric obstruction following the ingestion of commercial hydrochloric acid. The patient recovered following gastro-enterostomy.

The factors which influence the situation and type of gastric lesions are not clearly understood. The ingestion of acid even in small quantities or low concentration may be followed by the formation of scar tissue somewhere in the stomach without involving the esophagus. The ingestion of lye leads mainly to esophageal obstruction and only occasionally to gastric obstruction. The explanation given by Delore and Armand[5] is that lye, because of its greater concentration over the epithelial lining of the esophagus, inflicts a greater corrosive action at this site. Once this solution reaches the stomach, it is diluted rapidly and becomes innocuous. The acids, on the other hand, seem to have only a scorching effect on the esophageal mucosa and concentrate their effect on the pylorus. Samaja[6] believes this concentration to be due to tetanic contractures set up in the gastric wall.

CONCLUSION

The immediate effects of corrosive poisoning and the end results on the esophagus are well known and understood. However, little has been written in the pediatric literature of the late gastric lesions following corrosive poisoning and the purpose of this case report is to bring out the importance of careful observation of any infant that has swallowed corrosive liquids.

REFERENCES

1. Quenu, E.; and Petit, J.: Des stenoses cicatricielles du pylore consecutives a l'ingestion de liquides caustiques. Rev. de chir., **25**:51-67, 176-195, 1902.
2. Boikan, W. S.; and Singer, H. A.: Gastric Sequelae of Corrosive Poisoning. Arch. Int. Med., **46**:342 (Aug.) 1930.
3. Vinson, P. P.; and Hartman, H. R.: Pyloric Obstruction Due to Swallowing Solution of Concentrated Lye. Med. Clin. N. Amer., **8**:1037 (Jan.) 1925.
4. McLanahan, S.: Pyloric Occlusion Following the Ingestion of Corrosive Liquids. J.A.M.A., **102**:735 (March) 1934.
5. Delore and Armand, quoted by Elisher, E.: Pylorusstenosen hervorgernfen durch Salysauren and Aetzlaugen. Zentralbl. f. Chir., **50**:165 (Feb. 3) 1923.
6. Samaja, M.: Le stenosi cicatriziali del piloro secondarie ad ingestione di caustici. Reforma Med., **46**:202 (Feb. 10) 1930.

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PROTEINS OF THE BLOOD PLASMA

The work of Whipple and Robscheit-Robbins at the University of Rochester on foods which stimulate hemoglobin production, with the subsequent clinical studies of Minot and Murphy on pernicious anemia, gave a profound impulse to investigation of all the anemias, and in particular to studies of foods which favor red cell production in human beings.[1] The formation of the fluid portion of the blood, the plasma, has been less investigated. Albumin and globulin, its chief protein constituents, are vital in the nitrogen equilibrium of the body and in maintaining the osmotic pressure of the blood. Plasma protein disturbances have been observed in nephritis and edema and in various diseases. Human plasma protein is low in nephrosis, in uremia, in certain infections and often in pernicious anemia. Edema occurs at a low protein level.

Whether particular foods favor plasma protein formation has been little considered. Investigators[2] at the University of Rochester have recently extended the experimental technic used earlier there for hemoglobin studies; they have described a method applicable to quantitative investigation of the effect of foods on albumin and globulin regeneration in the fluid portion of the blood. Plasma protein of dogs was depleted by removal of whole blood and reinjection of red cells in Locke's solution, since it was desired to study protein regeneration in dogs which were not anemic. The procedure, plasmapheresis, was repeated daily to reduce the plasma protein content from the normal of 5 to 7 per cent to 4 per cent, at which point there is a strong stimulus to regenerate protein. At a lower level edema was likely to occur.

In human beings 6.8 to 8.8 per cent is given as the normal plasma protein level, with edema usually occurring at less than 5.5.[3] The plasma protein requirement of human blood is apparently higher than that of the dog.

The normal dog, say the Rochester workers, has a reserve circulating protein of 30 to 120 grams, depending upon the diet of the previous weeks. This means that he can regenerate as much protein as this from his tissues, without food. The reserve supply seems to be mainly in the liver, and it may be almost entirely depleted by fasting. The fasting dog can produce a considerable amount of new hemoglobin, presumably from tissue destruction. Although plasma protein is essential, during fasting the dog can produce only a very small amount. The body or tissue protein cannot contribute significantly to the circulating protein supply even in an emergency; though the opposite applies, and plasma injected into a dog's vein will keep him in nitrogen equilibrium. Protein in the blood will nourish the tissues; the flow may not be turned back so that the tissues nourish the blood during starvation.

Maintenance of the plasma protein level, essential to health, is dependent upon a steady supply of protein in the diet, and plant proteins are very effective. They usually favor the globulin fraction. Soy bean protein was promptly utilized and it favored the albumin rather than the globulin fraction. This is perhaps significant,

1. Editorial, Diet in Pernicious Anemia. THE JOURNAL, **20**: 168, 1927.

2. McNaught, J. B.; Scott, V. C.; Woods, F. M.; and Whipple, G. H.: Blood Plasma Protein Regeneration Controlled by Diet: Effects of Plant Protein Compared with Animal Protein and the Influence of Fasting and Infection. Jour. Exper. Med., **63**:277 (Feb.) 1936.

3. Nicholson, Daniel: Laboratory Medicine. Philadelphia: Lea & Febiger, 1934.

since albumin is the protein most frequently decreased in disease. No parallelism was observed between foods stimulating hemoglobin production and those which raised the plasma protein level. Hemoglobin regeneration appears to be favored by animal foods which do not particularly stimulate plasma protein formation. Plasma protein, which perhaps more closely resembles plant proteins than does hemoglobin, in the dog is more readily replaceable by these.

Infection and intoxication seriously interfered with protein regeneration, even when the food supply was adequate. In intoxication there is a large increase in the urinary nitrogen, which indicates body injury, and a sharp drop often occurs in the plasma protein level. In the studies of Whipple[2] and his associates there was some evidence to suggest that during anemia with low circulating protein, hemoglobin regeneration does not occur until after the plasma protein level has risen.

The relation of plasma protein to the sedimentation rate of red cells might be a matter of interest. The sedimentation rate is used as an index of the severity of an infection. The physical change from a high plasma protein concentration to a low, might influence the rate of settling of the blood cells.

Conditions favoring plasma protein increase are of sufficient importance to merit clinical analysis. The practical value of the Rochester work on hemoglobin inspires interest in the question of whether similar studies on plasma protein, as they are extended, may offer a comparable lead toward treatment of another nutritional disease.

GROWTH AFTER PROTEIN STARVATION

Protein furnishes the tissue building material, and protein deficiency is known to be particularly injurious to the young. Whether a period of severe protein deficiency during the growing period causes permanent damage, or whether the animal can recover completely on refeeding are questions which have been investigated recently.[1] From weaning to the age of fifteen weeks, or during more than a fourth of the developmental period, young rats received a ration high in fat and carbohydrate, adequate in minerals and vitamins, and practically free from protein. The controls received a supplement of milk protein, milk powder, and whole wheat.

The test animals seemed healthy, but showed a progressive emaciation, the weight remaining practically stationary. A number of deaths occurred, chiefly during the last weeks of deficiency. Pneumonia and enteritis were the most frequent causes; infection was rather common among the experimental animals. A large number of nutritional and endocrine factors apparently are capable of reducing the resistance of the tissues to invading micro-organisms.

There was a notable difference in the male and female mortality rate. Among the males, 35 per cent died; among the females only 14 per cent. At the end of the period of underfeeding, that is, when the animals were eighteen weeks old, they were returned to a full diet, and immediately resumed growth. The rate of gain then exceeded that of the controls, so that at the end of nine months the female test animals were as heavy as the female controls. The male gain was not quite so rapid as the female. The males were, however, almost as large as the male controls, and were still growing, so possibly would have overtaken the controls had they not been sacrificed at this time. Both male and female test animals were fertile and females showed normal estral cycles after refeeding, despite the period without protein.

Some differences of test and control rats were noted at autopsy. The experimental males were a little shorter than the controls, and the head, eyeballs and skeleton were lighter. In the females the eyeballs, humerus and femur were significantly lighter. The liver and spleen were heavier.

The females withstood protein starvation better than the males, since they showed a higher survival rate and recovered more rapidly on refeeding. It is of interest that though the animals on refeeding became very nearly normal in weight and body size, such a complex organ as the eyeball was apparently permanently smaller.

The female of practically every species is smaller than the male. This may be because she instinctively takes less food, or because of a forced adaptation to scarcity. Among human beings protein is the most costly article of diet and in primitive countries the male is usually preferentially fed. In the future social order profound changes may result from the civilized custom of equal rations for girls and boys.

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1. Jackson, C. M.: Recovery in Rats upon Refeeding after Prolonged Suppression of Growth by Dietary Deficiency of Protein. Amer. Jour. Anat., 58:179 (Jan.) 1936.

GLEANINGS FROM RECENT JOURNALS

Immunity to Poliomyelitis.—The epidemic of infantile paralysis last summer came shortly after rather wide publicity had been given to the possibilities of two new vaccines, that of Kolmer, of Philadelphia, and of Brodie, of New York.[1] A considerable number of children in the epidemic areas were inoculated with these two products despite some expressed uncertainty as to their value or safety. The percentage of immunization achieved cannot be determined, since the vaccinated children may not be inoculated or exposed to the disease, and it is believed that immune bodies in the blood are not a measure of resistance to this disease.

A recent detailed study from the Rockefeller Institute[2] on the vaccination of monkeys with three different viral preparations should give a clearer evaluation of their effects. The vaccines employed were the two above mentioned, that is, Kolmer's living ricinoleated virus, Brodie's formalin killed virus, and a third tannin precipitated living virus. Among a group of monkeys which received the Kolmer vaccine, one developed poliomyelitis; another after three injections did not resist intracerebral inoculation of the virus, thus was not immunized. In inoculations of living virus, say Olitsky and Cox, too little produces an inconstant immunity, too much produces infection; and there has been little progress since Flexner and Lewis said twenty-five years ago that killed virus did not protect, that with the living virus too little produced an inconstant immunity and too much produced the disease.

In reported epidemics of poliomyelitis, according to Lumsden,[3] the symptoms are often so different that it is possible that more than one disease is being considered.

Infantile paralysis has been compared to diphtheria, in that slight natural infections are believed gradually to immunize a considerable proportion of the population. The first successful prevention of diphtheria was by use of toxin-antitoxin mixtures, because neither the diphtheria organism nor its toxin could be administered alone. Preventive inoculations of polio virus and antiserum are reported as unsatisfactory.[1] Vaccination against yellow fever, rabies and smallpox, three other virus diseases, has been accomplished by inoculation of attenuated organisms. Bacterial prophylactic measures have been exceedingly ingenious, and each method has required a tremendous amount of laboratory experimentation for its successful development. Prevention of infantile paralysis continues to occupy the attention of many investigators.

Ovarian and Pituitary Hormones.—The various hormones obtainable from pregnancy urine and other sources have been widely tried in clinical medicine. A few conditions are emerging as probably benefited. The weight of evidence suggests that the undescended testicle may be brought into its normal position by prolonged injections of anterior pituitary-like sex hormone;[2] and that theelin is beneficial in gonococcal vulvovaginitis of children, though this has also been disputed.[3] In particular, menstrual and ovarian disorders have been extensively treated with the ovarian and pituitary hormones.

According to Hamblen and Ross,[4] who studied human ovaries at operation after injections of anterior pituitary-like sex hormone, degenerative changes seem to be induced in the follicles by this product, which probably does not induce ovulation in the human being as it does in the rat, rabbit and other small animals. Hamblen and Thomas,[5] in this issue of the JOURNAL, report the effects of various medical treatments upon endometrial hyperplasia and uterine bleeding.

For standardizing the ovarian and pituitary preparations, studies of the physiologic effects upon animals are invaluable. After the drugs are standardized the clinical effects are still completely unknown and to be discovered by the trial and error method. Careful observation and clinical reports such as the above are essential to the development of hormone therapy.

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1. Editorial, Poliomyelitis Vaccine. Sou. Med. Jour., **28**:286 (March) 1935.

Ibid: Studies on Poliomyelitis, p. 860, September.

2. Olitsky, P. K.; and Cox, H. R.: Experiments on Active Immunization Against Experimental Poliomyelitis. Jour. Exper. Med., **63**:109 (Jan.) 1936.

3. Lumsden, L. L.: Epidemiological Principles. Sou. Med. Jour., p. 303, this issue.

1. Rhoads, C. P.: Jour. Exper. Med., **53**:115, 1931. Schultz, E. W.: Jour. Pediat., **6**:615, 1935. Goodpasture, E. W.: Communication to Editor.

2. Editorial, Effects upon Boys of Large Doses of Gonadotropic Hormone. THE JOURNAL, **29**:214 (Feb.) 1936.

3. Witherspoon, J. Thornwell: Treatment of Gonorrheal Vulvovaginitis in Childhood with the Ovarian Follicular Hormones: Series of Cases in which Treatment was Unsuccessful. Amer. Jour. Dis. Child., **50**:913 (Oct.) 1935.

4. Hamblen, E. C.; and Ross, R. A.: A Study of Ovaries Following Preoperative Administration of an Extract of Pregnancy Urine. Amer. Jour. Obst. & Gyn., **31**:14 (Jan.) 1936.

5. Hamblen, E. C.; and Thomas, W. L., Jr.: Hyperplasia of Endometrium: A Study of Endometrium after Treatment. THE JOURNAL, this issue, p. 269.

Effect of Uterus on Ovary. — Hysterectomy in the rabbit may cause preservation of a functioning corpus luteum, like that found in pregnancy.[1] It would appear that the uterus has a function in the ovarian cycle of this species, either producing an internal secretion or in some way interfering with the ovarian cycle. A corollary is that a malfunctioning uterus which is usually thought of as the result of an ovarian disorder might initiate the ovarian disease.

TWENTY-FIVE YEARS AGO

From Journals of 1911

Origin of Referred Practice?[2]—"To the Editor: I wish to contribute a statement to the subject of the remuneration of physicians:

"I have been in the general practice of medicine since 1890 in Detroit on the same lot on which I was born. For twenty years I trusted all applicants for medical aid with results approximately as follows:

"2 per cent would pay me promptly.

"13 per cent could pay me only 'when I went after them.'

"25 per cent got out of paying me in every possible way.

"60 per cent did not pay me at all.

"January 1, 1910, I turned over a new leaf and referred to other physicians all would-be patients who did not pay cash and had not approved credit. In 1910 the income from my practice was 98 per cent greater than my average yearly income for the preceding twenty years, and my expenses for 1910 were less than the average yearly expenses for the same period. Except for the fact that I gave my individual attention to my invalid mother for the three years prior to 1908, which cut into my practice considerably, I am unable to assign any other cause than this change of policy for the increase in income.

"Since January 1, 1910, I have had more time for reading, refreshment and sleep; and my present plan is preferable to that of those physicians whose ambition is to have the "largest practice" in a community at the cost of poor health or an early death.

"John L. Irwin, M.D., Detroit."

The Testimonial as Evidence of Value of a Drug.[3]—"It is reported that United States District Attorney Sims has obtained a ruling from the Federal courts barring testimonials as evidence in those cases in which the question of the curative properties of patent medicines are before the courts. * * * Week in and week out, for years past, the *Journal* has persistently and consistently maintained that testimonials from laymen regarding the curative value of medicine or medical appliances are intrinsically worthless and scientifically valueless. * * *

"Every physician knows that a large proportion of those who are sick, or who think they are sick, will recover whether they receive treatment or not. * * *

"Speaking generally, it may be said that in all my experience in this office never has a medical concern, no matter how fraudulent its methods or worthless its treatment, been unable to produce an almost unlimited number of these so-called testimonial letters."

Apparently Describing Sickle Cell Anemia.[1]—"This patient has been under observation, at intervals, since 1907. She is a negress, aged 25, a native of southwestern Virginia, and has lived there all her life. When first seen, October 25, 1910, she complained of weakness, soreness and pain in the left side, and a sore on the left leg. She has never had good health. * * *

"Blood examination April, 1909, showed: red cells, 2,000,000; white cells, 11,000; hemoglobin (Sahli), 50 per cent. Differential white count was as follows: polymorphonuclears, 63 per cent; small mononuclears, 25 per cent; eosinophils, 4 per cent; mast cells, 6 per cent. The red cells showed poikilocytes in a variety of shapes, the most common variety being of a crescent shape. At several subsequent examinations cells of the same shape were found."

Alkalis and Hexamethylenamin in Pyelitis.[2]—"The course of the disease if untreated is essentially chronic. * * *

"The main and the only essential treatment consists in rendering the urine neutral, when passed, by the administration of alkaline remedies as speedily as possible, and in keeping it so until all the symptoms have disappeared. * * * The pain and uneasiness rapidly vanish and the temperature falls to normal within three days. The pus cells also disappear. The bacteria, however, may persist for a long time after the pus has gone; but they seem to do no harm. * * * The alkaline treatment must be continued for a week or two at least, in spite of the depressing effect which it has on the child's general condition and the loss of appetite which it is apt to occasion. If it is stopped too soon the symptoms return.

"Nearly all German and American clinicians depend on urinary antiseptics, hexamethylenamin (urotropin) and phenyl salicylate (salol), as of first value, and recommend alkaline drinks as of value in diluting and possibly alkalinizing the urine."

Hexamethylenamin in Poliomyelitis.[3] — Flexner and Clark found that if the drug hexamethylenamin be given so that it be present in the spinal fluid of a monkey and its administration be continued by mouth, injection of the virus intracerebrally resulted in some of the animals but not in all, first, in a prolongation

1. Loeb, Leo; and Smith, M. G.: Effect of Hysterectomy on the Duration of Life and Retrogression of the Corpora Lutea and on the Secondary Sex Organs of the Rabbit. Amer. Jour. Anat., **58**:1 (Jan.) 1936.

2. Correspondence, J.A.M.A., **56**:687, 1911.

3. Editorial, The Testimonial. J.A.M.A., **56**:673, 1911.

1. Washburn, R. F.: Virginia Medical Semi-Monthly, Richmond, Feb. 10. Abst., J.A.M.A., **56**:699, 1911.

2. Brenneman, Joseph: Purulent Infections of the Urinary Tract in Infancy. J.A.M.A., **56**:632-634, 1911.

3. Editorial, Important Recent Contributions to Our Knowledge of Poliomyelitis. J.A.M.A., **56**:671-2, 1911.

of the period of incubation from six or eight days to twenty-four days; and, next, in the prevention of paralysis.

"The results obtained in the use of hexamethylenamin in inhibiting, in a certain proportion of cases, the onset of paralysis, suggest the possibility of the use of this drug in serious outbreaks of the disease as a prophylactic."

Hookworm at Louisiana State University.[1]—"Following the investigation made by Dr. A. S. J. Hyde, of the Hookworm Commission, it is announced that 25 per cent of the students thus far examined at the State University are infected with hookworm."

1. Medical News: J.A.M.A., **56**:575, 1911.

Book Reviews

Infant Nutrition. A Text-book of Infant Feeding for Students and Practitioners of Medicine. By William McKim Marriott, B.S., M.D., Professor of Pediatrics, Washington University School of Medicine, St. Louis. Second Edition. 431 pages, illustrated. St. Louis: The C. V. Mosby Company, 1935. Cloth, $4.50.

The second edition of this outstanding work on infant nutrition appears five years after publication of the first edition. A chapter on allergy has been added and others have been almost completely rewritten in order to conform to the rapid advances which have been made in recent years. The subjects of acidosis,alkalosis and anhydremia and their relation to diarrhea and vomiting are especially good. The same can be said of the chapters on feeding and nutritional disturbances. In fact, the book as a whole is so excellent and contains such a wealth of practical information that it is difficult to refrain from superlatives in describing it. It should by all means be in every physician's library, and most certainly should be a constant reference work for pediatricians.

Pediatric Treatment. A Manual of the Treatment of the Diseases of Infants and Children Designed as a Reference Work Especially for the General Practitioner and Physicians Entering the Field of Pediatrics. By Philip S. Potter, A.B., M.D., F.A.A.P., Formerly Instructor in Clinical Pediatrics at the Medical School of Syracuse University; Attending Pediatrician to the Berkeley General Hospital and to its Out-Patient Department. 578 pages. New York: The Macmillan Company, 1935. Cloth, $5.00.

This book, dealing with pediatric treatment, has been written for the young pediatrician and the general practitioner. The information given conforms with generally accepted methods. The first division deals with pediatric procedures such as nursing care. In the second division the subject of nutrition and feeding is covered. The third division deals with the diseases of the new born. Finally there is a division which takes up treatment by systems. Each disease is very briefly described and the accepted treatment is concisely outlined. This work will prove of value to the type of practitioner for whom it is intended.

Diseases of the Skin. By Frank Crozer Knowles, M.D., Professor of Dermatology, Jefferson Medical College. Third Edition, Thoroughly Revised. 640 pages, illustrated. Philadelphia: Lea & Febiger, 1935. Cloth, $6.00.

To keep or not to keep, that is the question. Whether to retain outworn but time-honored modes of therapy, backed by the prestige of some master long since dead, or resolutely to throw them in the waste basket—that is the problem that plagues every author of a book on diseases of the skin. Many writers of such books are overawed by tradition or overcome by conservatism, retaining in modern texts such treatments for, example, as that recommended by Unna for lupus vulgaris, which consists of thrusting thorns impregnated with certain drugs into affected areas.

Frank Crozer Knowles happily handles this dilemma. Outworn modes of diagnosis and treatment of purely historical interest he has in large part discarded. In their place, well described, appear methods of treatment which are scientific and up-to-date. His style is clear and easy, and this means much in any medical book. A large number of rare diseases are included. These, while efficiently described, very properly do not receive a disproportionately large space.

The practitioner of medicine will find this volume, now in its third edition, one of the best available on diseases of the skin. It is particularly to be recommended to the physician who wishes a reference work that is reliable, up-to-date, sufficiently comprehensive and easy to use.

New Pathways for Children with Cerebral Palsy. By Gladys Gage Rogers, Director of Robin Hood's Barn: A Camp School for Children with Cerebral Palsy; and Leah C. Thomas, Director of Therapeutics at Robin Hood's Barn. 167 pages, illustrated. New York: The Macmillan Company, 1935. Cloth, $2.50.

The spastic child is carefully studied and the emotions analyzed by competent observers and teachers. The title is somewhat misleading, in that it at first glance leads one to think of a book dealing with neurology, when in fact the substance of the book reveals personal studies of these children, and gives new pathways for their natural outlets, with suggestions for new discoveries. The book convinces the reader of the opportunities lying hidden within these children. The characters of the children described are moulded into interesting phases, and they are won over to greater opportunities. This book should be in every pediatrician's reference files and in all public and school libraries. Further, its presence there should be made known. It is a valuable book.

A Terminology of Operations of the University of Chicago Clinics. By Hilger Perry Jenkins, M.D. 100 pages. Chicago: The University of Chicago Press, 1935. Price, $1.00.

This small brochure outlines a method of setting up and operating a filing system in forming a surgical record library. The author points out that the names of operations are not entirely standard among different surgeons, and that by the use of the same nomenclature statistical studies will have added value and follow-up surveys will be more accurate. In giving terminology he also suggests that numbers may be given to each procedure. It would be well if the author would do this himself so that the numbers would also be standard for all index systems.

Southern Medical News

ST. LOUIS CLINICS

The St. Louis Clinics will hold its Spring Conference beginning Monday, April 27, and continuing throughout the entire week, at which time clinical demonstrations will be given daily from 8:30 a. m. to 12:00 noon and from 1:00 to 4:00 p. m. The regular program of the St. Louis Medical Society will be on Tuesday evening under the direction of the Clinics. On Monday and Wednesday afternoons from 4:00 to 5:00 demonstrations will be given by members of the Medical Reserve Officers of the Seventh Corps Area, U.S.A. A dinner will be given on Thursday evening. The program, which will be strictly clinical, will be presented entirely by St. Louis physicians. Registrants will be most cordially welcomed at all functions. For further information address Secretary, St. Louis Clinics, 3839 Lindell Boulevard, St. Louis, Missouri.

ALABAMA

Dr. James S. McLester, Birmingham, was a guest speaker before the Central Medical Society at Jackson, Mississippi, recently.

The University of Alabama School of Medicine, University, will have as speakers under the auspices of Phi Beta Pi, Professional Medical Fraternity, on March 13 and 14 Dr. L. B. Arey, Chicago, Illinois, and Dr. Roy R. Kracke, Emory University, Georgia.

Deaths

Dr. William T. Pride, Madison, aged 70, died recently.

Dr. William D. Lawrence, Gadsden, aged 74, died November 5 of pneumonia.

Dr. George Walter Gaillard, Perdue Hill, aged 78, died recently of bronchopneumonia and cerebral hemorrhage.

ARKANSAS

The Faulkner County Medical Society has elected the following officers for the coming year: Dr. I. N. McCollum, Conway, President; Dr. L. S. Dunaway, Conway, Vice-President; Dr. J. S. Westerfield, Conway, Secretary-Treasurer.

The Searcy County Medical Society has elected the following officers for the coming year: Dr. J. C. Pate, Bigflat, President; Dr. J. A. Henley, Marshall, Vice-President; Dr. S. G. Daniel, Marshall, Secretary-Treasurer.

The Madison County Medical Society has elected the following officers for the coming year: Dr. George D. Counts, Wesley, President; Dr. Fred Youngblood, Huntsville, Secretary-Treasurer.

The Miller County Medical Society has elected the following officers for the coming year: Dr. B. C. Middleton, Texarkana, President; Dr. Hugh Longino, Texarkana, Vice-President; Dr. R. R. Robins, Camden, Secretary-Treasurer.

The Monroe County Medical Society has elected the following officers for the coming year: Dr. W. L. Boswell, Clarendon, President; Dr. P. E. Terry, Holly Grove, Vice-President; Dr. M. L. Dalton, Brinkley, Secretary.

The Lincoln County Medical Society has elected the following officers for the coming year: Dr. R. L. Johnson, Grady, President; Dr. A. F. Williams, Vice-President; Dr. Vernon Tarver, Star City, Secretary-Treasurer.

The Fifth Councilor District Medical Society has elected the following officers for the coming year: Dr. S. A. Thompson, Camden, President; Dr. W. P. Cooksey, Magnolia, Vice-President; Dr. Berry Moore, El Dorado, Secretary-Treasurer.

Dr. W. J. Hunt, formerly of Poteau, Oklahoma, has opened offices in Warren.

Dr. E. J. Byrd, formerly of Bearden, has moved to Fordyce.

Dr. J. M. Wallace, formerly of Fayetteville, has moved to Harrison.

Dr. W. H. Estes, formerly of Cushman, has moved to Sage.

Dr. J. G. Gladden, Harrison, was recently appointed a member of the State Board of Health.

Dr. O. J. T. Johnston has been made President of the Batesville Kiwanis Club.

Dr. H. H. McAdams, Jonesboro, has been appointed a member of the School Board of that city.

Dr. H. E. Murry, Texarkana, has been made a Director of the Kiwanis Club of that city.

Dr. W. W. Brown, Williford, and Miss Margaret McLeod were married recently.

Deaths

Dr. William Starling Bradford, Harrisburg, aged 75, died November 25 of heart disease.

Dr. Charles S. Crockett, Lincoln, aged 58, died December 7 of myocarditis.

DISTRICT OF COLUMBIA

Dr. John S. Arnold, Washington, has resigned from the Health Department to enter private practice.

Dr. Archibald Barklie Coulter, Washington, has been appointed Director of Tuberculosis of the Health Department of the District of Columbia.

Deaths

Dr. Charles McDuffy Wilder, Washington, aged 41, died November 27 of subacute bacterial endocarditis following an accidental abrasion of his hand.

Dr. Henry Harrison Hibsman, Washington, aged 48, died November 18 of angina pectoris.

Dr. Orwin E. Howe, Washington, aged 82, died recently.

Dr. Isaac Scott Stone, Washington, aged 84, died December 22.

FLORIDA

Dr. Luther W. Holloway, Jacksonville, has been appointed a member of the Council of the Southern Medical Association from Florida for a regular Council term of five years, the appointment having been announced recently by the President, Dr. Fred M. Hodges, of Richmond. Dr. Holloway succeeds Dr. Edward Jelks, Jacksonville, who, having served the constitutional limit, was not eligible for reappointment.

The St. Johns County Medical Society has elected the following officers for the coming year: Dr. Herbert E. White, St. Augustine, President; Dr. George W. Potter, St. Augustine, Vice-President; Dr. R. D. Harris, St. Augustine, Secretary; Dr. A. Clark Walkup, St. Augustine, Treasurer.

The Pasco-Hernando-Citrus County Medical Society has elected the following officers for the coming year: Dr. R. D. Sistrunk, Dade City, President; Dr. S. C. Harvard, Brooksville, First Vice-President; Dr. P. J. Hudson, Crystal River, Second Vice-President; Dr. J. J. Bourke, Dade City- Secretary-Treasurer.

The Lee County Medical Society elected the following officers for the coming year: Dr. W. H. Grace, Fort Myers, President; Dr. R. D. Newton, Fort Myers, Vice-President; Dr. H. Quillian Jones, Fort Myers, Secretary-Treasurer.

The Escambia County Medical Society elected the following officers for the coming year: Dr. A. M. Ames, Pensacola, President; Dr. J. I. Turberville, Century, Vice-President; Dr. J. M. Hoffman, Pensacola, Secretary-Treasurer.

The Columbia County Medical Society elected the following officers for the coming year: Dr. L. M. Anderson, Lake City, President; Dr. R. B. Harkness, Lake City, Vice-President; Dr. T. H. Bates, Lake City, Secretary-Treasurer.

Dr. Louie Limbaugh, Jacksonville, was recently appointed Chief of the Department of Medicine at Duval County Hospital, succeeding Dr. R. H. McGinnis, resigned.

Deaths

Dr. John Walter Hodges, Miami, aged 78, died November 27 of nephritis.

Dr. Ira L. Blanton, MacClenny, aged 49, died November 6 of uremia.

GEORGIA

The Baldwin County Medical Society has elected the following officers for the coming year: Dr. S. A. Anderson, Milledgeville, President; Dr. L. S. Bailey, Milledgeville, Vice-President; Dr. C. B. Fulghum, Milledgeville, Secretary-Treasurer.

The Cherokee County Medical Society has elected the following officers for the coming year: Dr. R. M. Moore, Waleska, President; Dr. N. J. Coker, Canton, Vice-President; Dr. George C. Brooke, Canton, Secretary-Treasurer.

The Clayton-Fayette Counties Medical Society has elected the following officers for the coming year: Dr. E. C. Seawright, Fayetteville, President; Dr. J. R. Wallace, Lovejoy, Vice-President; Dr. T. J. Busey, Fayetteville, Secretary-Treasurer.

The Coffee County Medical Society has elected the following officers for the coming year: Dr. J. G. Crovatt, Douglas, President; Dr. T. H. Johnston, Douglas, Secretary-Treasurer.

The Dougherty County Medical Society has elected the following officers for the coming year: Dr. Alex R. Freeman, Albany,

Continued on page 24

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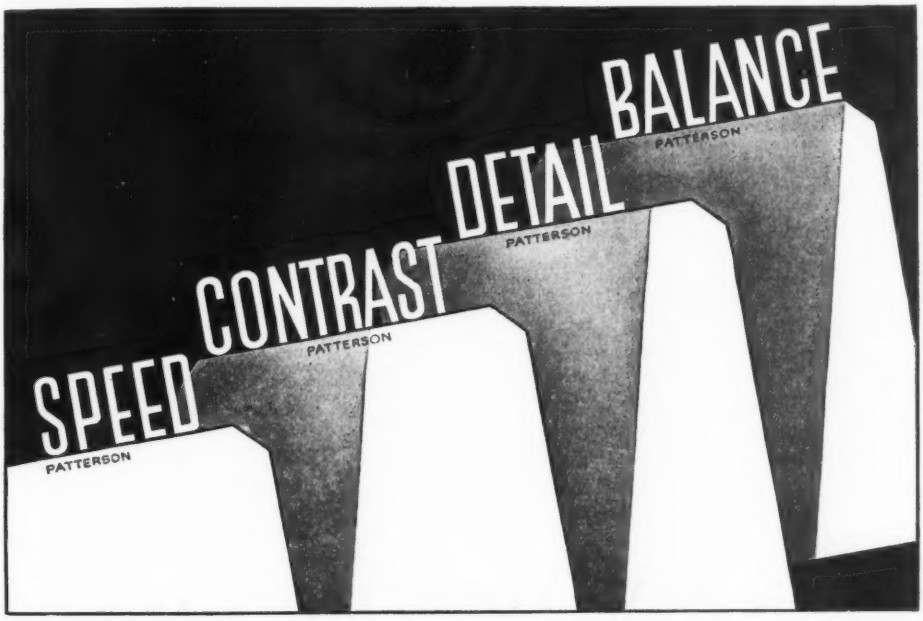

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Continued from page 338

President; Dr. Frank E. Thomas, Albany, Vice-President; Dr. I. M. Lucas, Albany, Secretary-Treasurer.

The Fulton County Medical Society has elected the following officers for the coming year: Dr. Grady E. Clay, Atlanta, President; Dr. H. C. Sauls, Atlanta, President-Elect; Dr. George F. Eubanks, Atlanta, Vice-President; Dr. M. T. Harrison, Atlanta, Secretary-Treasurer.

The Georgia Medical Society has elected the following officers for the coming year: Dr. C. F. Holton, Savannah, President; Dr. George H. Faggart, Savannah, President-Elect; Dr. S. E. Bray, Savannah, Vice-President; Dr. Otto W. Schwalb, Savannah, Secretary-Treasurer.

The Habersham County Medical Society has elected the following officers for the coming year: Dr. Robert B. Lamb, Demorest, President; Dr. H. E. Crow, Alto, Vice-President; Dr. O. N. Harden, Cornelia, Secretary-Treasurer.

The Hall County Medical Society has elected the following officers for the coming year: Dr. E. W. Grove, Gainesville, President; Dr. J. M. Hulsey, Gainesville, Vice-President; Dr. Hartwell Joiner, Gainesville, Secretary-Treasurer.

The Randolph County Medical Society has elected the following officers for the coming year: Dr. Loren Gary, Jr., Shellman, President; Dr. E. C. McCurdy, Shellman, Vice-President; Dr. W. G. Elliott, Cuthbert, Secretary-Treasurer.

The Richmond County Medical Society has elected the following officers for the coming year: Dr. Edgar R. Pund, Augusta, President; Dr. J. H. Sherman, Augusta, Vice-President; Dr. R. C. McGahee, Augusta, Secretary-Treasurer.

The Thomas County Medical Society has elected the following officers for the coming year: Dr. Harry Ainsworth, Thomasville, President; Dr. J. N. Isler, Meigs, Vice-President; Dr. Rudolph Bell, Thomasville, Secretary-Treasurer.

The Spalding County Medical Society has elected the following officers for the coming year: Dr. T. I. Hawkins, Griffin, President; Dr. George L. Walker, Griffin, Vice-President; Dr. H. J. Copeland, Griffin, Secretary-Treasurer.

The Third District Medical Society has elected the following officers for the coming year: Dr. J. E. Walker, Columbus, President; Dr. R. M. Ware, Fitzgerald, Vice-President; Dr. Charles A. Greer, Oglethorpe, Secretary (for life).

The Tri County Medical Society has elected the following officers for the coming year: Dr. E. B. Baughn, Colquitt, President; Dr. C. R. Barksdale, Blakely, Vice-President; Dr. J. G. Standifer, Blakely, Secretary-Treasurer.

The Walker County Medical Society has elected the following officers for the coming year: Dr. R. M. Coulter, LaFayette, President; Dr. C. W. Stephenson, Ringgold, Vice-President; Dr. Charles W. Folsom, LaFayette, Secretary-Treasurer.

The Whitfield County Medical Society has elected the following officers for the coming year: Dr. E. O. Shellhorse, Dalton, President; Dr. F. B. Easley, Dalton, Vice-President; Dr. H. J. Ault, Dalton, Secretary-Treasurer.

Dr. Eugene E. Murphey, Augusta, has been named Commissioner Emeritus of the Board of Health of that city.

Dr. Lon Grove, Atlanta, has been made President of the Staff of Wesley Memorial Hospital.

Dr. F. C. Mims, Atlanta, was recently made Worshipful Master of the Morningside Masonic Lodge.

Dr. Joseph C. Read, Atlanta, has opened offices in the Medical Arts Building.

Dr. Leonard Julius Rabhan, Savannah, and Miss Belle Sawilowsky were married December 25.

Dr. Clyde Findley Bowie, Atlanta, and Miss Bessie M. Crary were married recently.

Deaths

Dr. Marion W. Jinks, Suwanee, aged 66, died December 8 of acute nephritis.

Dr. Robert Berrien Ridley, Atlanta, aged 56, died December 4 of heart disease.

Dr. James Robert Cranford, Sasser, aged 65, died November 29.

Dr. Marion Cicero McClain, Marble Hill, aged 76, died December 25.

KENTUCKY

The Whitley County Medical Society has elected the following officers for the coming year: Dr. L. L. Terrell, Corbin, President; Dr. William Cox, Corbin, Vice-President; Dr. C. A. Moss, Williamsburg, Secretary-Treasurer.

The Greenup County Medical Society elected the following officers for the coming year: Dr. J. A. Franz, Russell, President;

Continued on page 26

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SPECIAL COURSES:

Otolaryngology and Ophthalmology—March 2 to March 14, 1936.

Surgery, Gynecology and Obstetrics—May 11 to June 6, 1936.

Tropical Medicine and Parasitology—June 15 to July 25, 1936.

COURSES leading to a higher degree are also given.

For bulletin furnishing detailed information address the

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Continued from page 24

Dr. H. T. Morris, Greenup, Vice-President; Dr. Carl M. Gambill, Greenup, Secretary-Treasurer.

The McCracken County Medical Society elected the following officers for the coming year: Dr. Warren P. Sights, Paducah, President; Dr. William Eaton, Paducah, Vice-President; Dr. Leon Higdon, Paducah, Secretary; Dr. E. W. Jackson, Paducah, Treasurer.

The Jefferson County Medical Society, Louisville, had as guest speaker at a recent meeting Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania.

DEATHS

Dr. James T. Morris, Stanford, aged 74, died recently of heart disease.

Dr. Joel Bartelson Million, Newby, aged 56, died November 19.

Dr. Wade Moss Gibson, Richmond, aged 60, died recently of chronic myocarditis, thrombophlebitis of both legs and ulcer of the stomach.

Dr. Gustavus Dedman Lillard, Lawrenceburg, aged 70, died November 24 of coronary embolism.

Dr. Solomon Milton Linville, Lexington, aged 55, died recently of coronary thrombosis.

Dr. Edgar Boston Driskell, Worthville, aged 54, died November 30 of injuries received when struck by an automobile.

Dr. David Allen Crosby, Lexington, aged 71, died December 23 from injuries received in an automobile accident.

LOUISIANA

The Orleans Parish Medical Society elected the following officers for the coming year: Dr. Frederick L. Fenno, New Orleans, President; Dr. Foster M. Johns, New Orleans, First Vice-President; Dr. Edwin L. Zander, New Orleans, Second Vice-President; Dr. J. Raymond Hume, New Orleans, Third Vice-President; Dr. Gilbert C. Anderson, New Orleans, Secretary.

The DeSoto Parish Medical Society has elected the following officers for the coming year: Dr. W. G. Jones, Mansfield, President; Dr. B. P. Smith, Keatchie, Vice-President; Dr. R. A. Tharp, Mansfield, Secretary-Treasurer.

The Shreveport Medical Society elected the following officers for the coming year: Dr. C. P. Rutledge, President; Dr. J. A. Wilkinson, First Vice-President; Dr. W. J. Norfleet, Second Vice-President; Dr. P. D. Abramson, Secretary; Dr. D. R. McIntyre, Treasurer.

Dr. A. H. Deekens, formerly of Kilmarnock, Virginia, has located in New Orleans.

DEATHS

Dr. Lucien Eldred Larche, Bastrop, aged 51, died in December of pneumonia.

Dr. Cullen Clarence Conerly, Fisher, aged 56, died December 1 of carcinoma of the stomach.

MARYLAND

Dr. William Mansfield Clark, Baltimore, Professor of Physiological Chemistry, Johns Hopkins University School of Medicine, was awarded the William H. Nichols Medal of the New York Section of the American Chemical Society for 1936.

DEATHS

Dr. William Burdick, Baltimore, aged 64, died December 21.

Dr. George Lawson Wilkins, Baltimore, aged 84, died December 14 of bronchopneumonia.

MISSISSIPPI

The Clarksdale and Six Counties Medical Society had as guest speaker at a recent meeting Dr. Eugene Rosamond, Memphis, Tennessee.

DEATHS

Dr. William Krauss, Meridian, aged 74, died December 21 of carcinosis.

Dr. Archibald McCallum, Gulfport, aged 80, died recently of chronic myocarditis.

MISSOURI

The Buchanan County Medical Society has elected the following officers for the coming year: Dr. J. M. Allaman, St.

Continued on page 28

When Cardiac Disease Is Suspected

IN many cases where symptoms suggest cardiac disease, accuracy of conclusions cannot always be assumed if they are based on clinical findings alone. Yet positive diagnosis and prompt treatment are necessary to conserve the patient's health and life.

A radiographic study should be a part of the examining routine. The heart's silhouette, as shown by the radiograph, is a reliable index to its condition. For the heart's size, shape, and position often are directly affected by its anatomical and functional status.

Thus, radiography aids in determining pathology and is equally valuable as a means of excluding heart disease if not present even though symptoms may point to it. To be certain your findings are complete and accurate, refer the patient to a radiologist in all cases of suspected cardiac disease.

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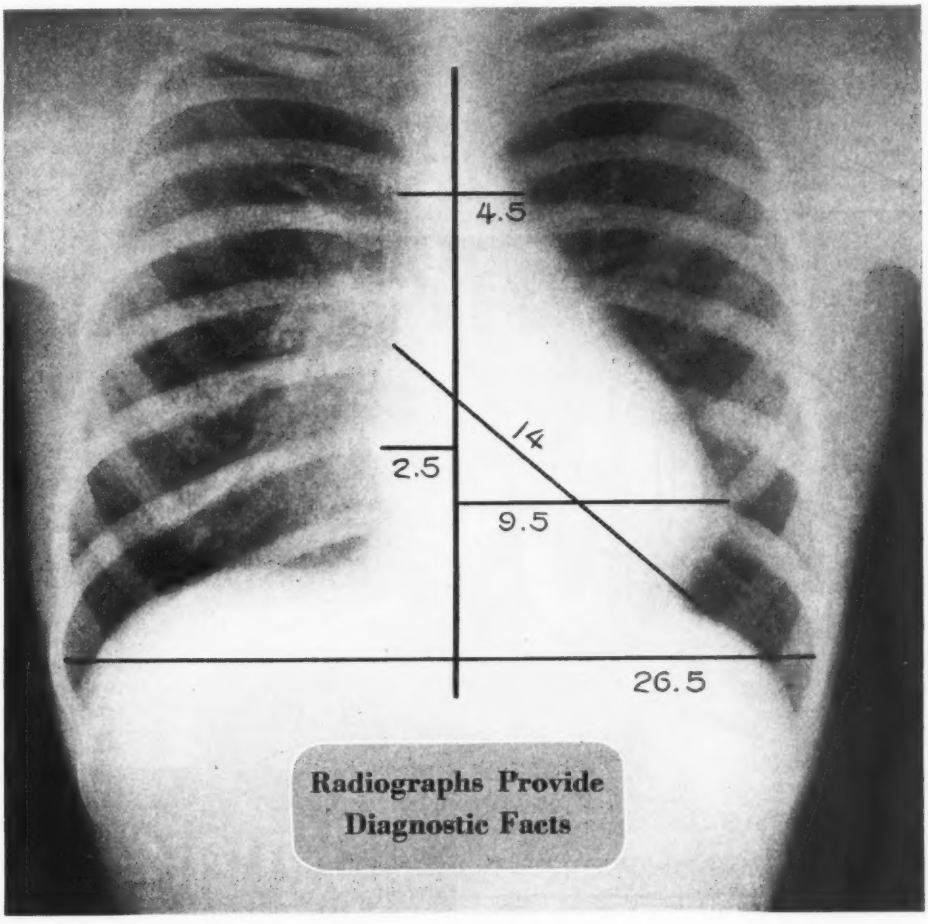

Continued from page 26

Joseph, President; Dr. J. T. Stamey, St. Joseph, Vice-President; Dr. O. E. Whitsell, St. Joseph, Secretary; Dr. J. M. Bell, St. Joseph, Treasurer.

The Cape Girardeau County Medical Society has elected the following officers for the coming year: Dr. G. J. Tygett, Cape Girardeau, President; Dr. Rusby Seabaugh, Jackson, Vice-President; Dr. M. H. Shelby, Cape Girardeau, Secretary; Dr. B. W. Hays, Jackson, Treasurer.

The Lafayette County Medical Society has elected the following officers for the coming year: Dr. Francis W. Mann, Wellington, President; Dr. W. E. Koppenbrink, Higginsville, President-Elect; Dr. E. L. Johnston, Concordia, Secretary-Treasurer.

The Nodaway County Medical Society has elected the following officers for the coming year: Dr. Jack Rowlett, Maryville, President; Dr. L. E. Egley, Maryville, Vice-President; Dr. W. R. Jackson, Maryville, Secretary-Treasurer.

The Pettis County Medical Society has elected the following officers for the coming year: Dr. H. A. Hite, Green Ridge, President; Dr. Gordon Stauffacher, Sedalia, Vice-President; Dr. Edward H. Schaefer, Sedalia, Secretary; Dr. A. E. Monroe, Sedalia, Treasurer.

The Randolph-Monroe County Medical Society has elected the following officers for the coming year: Dr. M. C. McMurry, Paris, President; Dr. T. S. Fleming, Moberly, Vice-President; Dr. M. E. Kaiser, Moberly, Secretary-Treasurer.

The Saline County Medical Society has elected the following officers for the coming year: Dr. J. R. Lawrence, Marshall, President; Dr. S. T. Mead, Slater, Vice-President; Dr. R. C. Gentry, Sweet Springs, Secretary.

The South Central Counties Medical Society has elected the following officers for the coming year: Dr. A. H. Thornburgh, West Plains, President; Dr. R. A. Ryan, Mountain Grove, Vice-President; Dr. A. C. Ames, Mountain Grove, Secretary-Treasurer.

The Kansas City Pathological Society has elected the following officers for the coming year: Dr. Frank J. Hall, Kansas City, President; Dr. R. W. Kerr, Kansas City, Secretary-Treasurer.

Deaths

Dr. Herman Benjamin Miller, St. Louis, aged 56, died November 16 of pneumonia.

Dr. Edward Morrish, St. Louis, aged 63, died November 27 of diabetes mellitus.

Dr. Harry Nelson Lutman, Versailles, aged 65, died recently of cerebral hemorrhage.

Dr. Charles Edward Nickson, Independence, aged 62, died November 6 of heart disease.

Dr. Richard G. Callihan, Luray, aged 66, died November 28.

Dr. John Ellis Jennings, St. Louis, aged 73, died December 5 of pneumonia.

NORTH CAROLINA

The Randolph County Medical Society has elected the following officers for the coming year: Dr. C. S. Tate, Ramseur, President; Dr. W. L. Lambert, Ashboro, Vice-President; Dr. J. H. Soady, Ashboro, Secretary-Treasurer.

The Wake County Medical Society has elected the following officers for the coming year: Dr. Ivan Proctor, Raleigh, President; Dr. R. L. McGee, Vice-President; Dr. N. H. McLeod, Raleigh, Secretary-Treasurer.

Dr. C. F. Strosnider, Goldsboro, President of the North Carolina Medical Society, was a guest speaker before the faculty and students of Duke University School of Medicine, Durham, recently.

Dr. Mark T. Frizzelle, Ayden, was recently elected President of the Duke Alumni Association of Pitt County.

Dr. Milton J. Rosenau, formerly Charles Wilder Professor of Preventive Medicine and Hygiene at Harvard Medical School and in the Harvard School of Public Health, Boston, has been made Director of a new Division of Public Health at the University of North Carolina School of Medicine, Chapel Hill.

Dr. Alfred Blalock, Vanderbilt University School of Medicine, Nashville, Tennessee, was a guest speaker before the Duke University School of Medicine recently.

Dr. Charles N. Eckerson, formerly of Teaneck, New Jersey, has located at Cameron.

Continued on page 30

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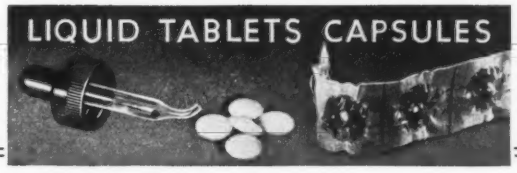

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Continued from page 28

Dr. John W. Bowdoin, Bloxom, was recently made Superintendent of Public Welfare for Accomac County.

Dr. A. D. Cregg, formerly Health Officer of Edgecombe County, has located at Liberty for the practice of medicine.

Dr. Herbert Flake Reading, Durham, and Miss Sara Whiteman were married December 22.

Dr. Ernest H. Reynolds and Miss Garnette Reynolds, both of Mayodan, were married December 14.

Dr. Allan Simpson Chrisman, Charlotte, and Miss Eleanore Krekeler were married December 21.

Dr. Oren Douglas Boyce, Charlotte, and Miss Virginia Wilkes were married recently.

DEATHS

Dr. William Dougal MacMillan, Vista, aged 91, died November 12 of arteriosclerosis and angina pectoris.

Dr. James J. Stewart, Mt. Holly, aged 59, died January 1.

Dr. Arthur Ogburn Spoon, Greensboro, aged 54, died December 10.

OKLAHOMA

The Choctaw County Medical Society has elected the following officers for the coming year: Dr. W. N. John, Hugo, President; Dr. R. L. Gee, Hugo, Vice-President; Dr. E. A. Johnson, Hugo, Secretary-Treasurer.

The Garvin County Medical Society has elected the following officers for the coming year: Dr. Charles M. Pratt, Lindsay, President; Dr. C. L. Sullivan, Elmore City, Vice-President; Dr. John R. Callaway, Pauls Valley, Secretary-Treasurer.

The Jefferson County Medical Society has elected the following officers for the coming year: Dr. J. I. Derr, Waurika, President; Dr. F. M. Edwards, Ringling, Vice-President; Dr. J. I. Hollingsworth, Waurika, Secretary-Treasurer.

The Muskogee County Medical Society has elected the following officers for the coming year: Dr. C. M. Fullenwider, Muskogee, President; Dr. W. R. Jobin, Porter, Vice-President; Dr. S. D. Neely, Muskogee, Secretary-Treasurer.

The Okmulgee-Okfuskee County Medical Society has elected the following officers for the coming year: Dr. J. C. Matheney, Okmulgee, President; Dr. G. Y. McKinney, Henryetta, Vice-President; Dr. M. B. Glismann, Okmulgee, Secretary-Treasurer.

The Osage County Medical Society has elected the following officers for the coming year: Dr. G. I. Walker, Hominy, President; Dr. G. K. Hemphill, Pawhuska, Vice-President; Dr. J. F. Daly, Pawhuska, Secretary-Treasurer.

The Pittsburg County Medical Society has elected the following officers for the coming year: Dr. B. B. Kies, McAlester, President; Dr. Claude E. Lively, McAlester, Vice-President; Dr. L. C. Kuyrkendall, McAlester, Secretary-Treasurer.

The Rogers County Medical Society has elected the following officers for the coming year: Dr. J. C. Bushyhead, Claremore, President; Dr. K. D. Jennings, Chelsea, Vice-President; Dr. W. A. Howard, Chelsea, Secretary-Treasurer.

The Stephens County Medical Society has elected the following officers for the coming year: Dr. Berry H. Burnett, Duncan, President; Dr. E. King, Duncan, Vice-President; Dr. D. Long, Duncan, Secretary.

The Wagoner County Medical Society has elected the following officers for the coming year: Dr. S. R. Bates, Wagoner, President; Dr. J. H. Plunket, Wagoner, Vice-President; Dr. John D. Leonard, Wagoner, Secretary.

Dr. J. Samuel Binkley, formerly of Oklahoma City, has located in New York City.

Dr. B. W. Slover, formerly of Blanchard, has moved to Granite.

DEATHS

Dr. Lord Byron Barnes, Tulsa, aged 50, died in November.

Dr. James Edward Davis, McAlester, aged 56, died December 20 as the result of injuries received in an automobile accident.

SOUTH CAROLINA

Dr. Kenneth M. Lynch, Charleston, has been appointed a member of the Council of the Southern Medical Association from South Carolina for a regular Council term of five years, the appointment having been announced recently by the President, Dr. Fred M. Hodges, of Richmond. Dr. Lynch succeeds Dr. Frank H. McLeod, of Florence, who, having served the constitutional limit, was not eligible for reappointment.

The Columbia County Medical Society has elected the follow-

Continued on page 32

INFANT FEEDING PROBLEMS
The Baby won't eat
WHEN determination of the cause or causes producing anorexia reveals the necessity for dietary readjustment . . . the choice of a milk modifier to a large extent is dependent upon its contribution to ease of digestion, rapidity of assimilation and pleasantness of taste. This holds true regardless of whether underfeeding or previous overfeeding or an imperfectly balanced formula is the cause of the anorexia.
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Continued from page 30

ing officers for the coming year: Dr. Theo. M. DuBose, Jr., Columbia, President; Dr. David Adcock, Columbia, Vice-President; Dr. Benjamin Rubinowitz, Columbia, Secretary; Dr. Thomas Dotterer, Columbia, Treasurer.

The Oconee County Medical Society has elected the following officers for the coming year: Dr. W. C. Mays, Fair Play, President; Dr. J. T. Davis, Walhalla, Vice-President; Dr. E. A. Hines, Seneca, Secretary.

The Pitt County Medical Society has elected the following officers for the coming year: Dr. S. M. Crisp, Greenville, President; Dr. W. M. B. Brown, Greenville, Vice-President; Dr. W. K. McDowell, Greenville, Secretary-Treasurer.

Dr. James H. Hutchison, Columbia, and Miss Hildegarde Schroder were married recently.

Dr. Edward Sinton Cardwell, Columbia, and Miss Lily Mikell Legare were married November 29.

Dr. Benjamin Rubinowitz, Columbia, and Miss Lucy Mae Felker were married December 26.

Deaths

Dr. Samuel Eugene Harmon, Columbia, aged 64, died December 26 of coronary thrombosis.

Dr. James Carlisle Moore, McColl, aged 57, died December 13 of angina pectoris and pulmonary embolism.

Dr. Matilda Arabelle Evans, Columbia, aged 66, died November 17 of nephritis and cerebral hemorrhage.

TENNESSEE

The Bradley County Medical Society has elected the following officers for the coming year: Dr. J. L. McClary, Cleveland, President; Dr. W. C. Stansberry, Charleston, Vice-President; Dr. Claude Taylor, Cleveland, Secretary-Treasurer.

The Davidson County Medical Society has elected the following officers for the coming year: Dr. H. S. Shoulders, Nashville, President; Dr. H. L. Douglas, Nashville, Vice-President; Dr. J. P. Gilbert, Nashville, Secretary-Treasurer.

The Greene County Medical Society has elected the following officers for the coming year: Dr. N. H. Crews, Greeneville, President; Dr. R. S. Cowles, Greeneville, Vice-President; Dr. C. P. Fox, Jr., Greeneville, Secretary-Treasurer.

The Grundy County Medical Society has elected the following officers for the coming year: Dr. U. B. Bowden, Pelham, President; Dr. O. H. Clements, Palmer, Vice-President; Dr. T. F. Taylor, Monteagle, Secretary-Treasurer.

The Jackson County Medical Society has elected the following officers for the coming year: Dr. J. D. Quarles, Whitleyville, President; Dr. R. C. Gaw, Gainsboro, Vice-President; Dr. F. B. Clark, Gainesboro, Secretary-Treasurer.

The Knox County Medical Society has elected the following officers for the coming year: Dr. M. S. Roberts, Knoxville, President; Dr. John Smoot, Knoxville, Vice-President; Dr. Jesse C. Hill, Knoxville, Secretary-Treasurer.

The McMinn County Medical Society has elected the following officers for the coming year: Dr. R. W. Epperson, Athens, President; Dr. S. B. McClary, Jr., Etowah, Secretary-Treasurer.

The Montgomery County Medical Society has elected the following officers for the coming year: Dr. F. A. Martin, Clarkesville, President; Dr. R. M. Workman, Clarkesville, Vice-President; Dr. Philip Lyle, Clarkesville, Secretary-Treasurer.

The Polk County Medical Society has elected the following officers for the coming year: Dr. W. Y. Gilliam, Copperhill, President; Dr. W. C. Strauss, Copperhill, Vice-President; Dr. F. O. Geisler, Isabella, Secretary-Treasurer.

The Putnam County Medical Society has elected the following officers for the coming year: Dr. J. Fred Terry, Cookeville, President; Dr. W. A. Howard, Cookeville, Vice-President; Dr. Thurman Shipley, Cookeville, Secretary-Treasurer.

The Roane County Medical Society has elected the following officers for the coming year: Dr. F. D. Owings, Rockwood, President; Dr. T. L. Bowman, Rockwood, Vice-President; Dr. W. W. Hill, Harriman, Secretary-Treasurer.

The Robertson County Medical Society has elected the following officers for the coming year: Dr. W. F. Fyke, Springfield, President; Dr. E. W. Adair, Springfield, Vice-President; Dr. W. S. Rude, Ridgetop, Secretary-Treasurer.

The Memphis and Shelby County Medical Society has elected the following officers for the coming year: Dr. Robin F. Mason, Memphis, President; Dr. O. S. Warr, Memphis, President-Elect; Dr. F. W. Smythe, Memphis, Vice-President; Dr. A. F. Cooper, Memphis, Secretary; Dr. J. J. Hobson, Memphis, Treasurer.

The Sullivan and Johnson Counties Medical Society has elected the following officers for the coming year: Dr. W. H. Reed, Kingsport, President; Dr. D. D. Vance, Bristol, Vice-President

Continued on page 34

★ PYELITIS ★

Prompt relief of the distressing symptoms which often accompany pyelitis may be obtained by the oral administration of Pyridium. Shortening of the duration of treatment has been reported in many cases. Pyridium is non-toxic and non-irritative in therapeutic doses. Pyridium solution for kidney lavage may be employed effectively with the oral administration of the tablets.

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Continued from page 32

(Sullivan County); Dr. R. O. Glenn, Mountain City, Vice-President (Johnson County); Dr. T. R. Bowers, Bristol, Secretary-Treasurer.

The Washington County Medical Society has elected the following officers for the coming year: Dr. W. M. Bevis, Johnson City, President; Dr. J. L. Hankins, Johnson City, Vice-President; Dr. C. H. Long, Johnson City, Secretary-Treasurer.

The White County Medical Society has elected the following officers for the coming year: Dr. S. E. Gaines, Sparta, President; Dr. Vernon Hutton, Ravenscroft, Vice-President; Dr. A. F. Richards, Sparta, Secretary-Treasurer.

The Williamson County Medical Society has elected the following officers for the coming year: Dr. R. H. Hutchinson, Franklin, President; Dr. Knox Galloway, Franklin, Vice-President; Dr. K. S. Howlett, Franklin, Secretary-Treasurer.

The Wilson County Medical Society has elected the following officers for the coming year: Dr. L. L. Tilley, Lebanon, President; Dr. M. H. Wells, Watertown, Vice-President; Dr. R. B. Gaston, Lebanon, Secretary-Treasurer.

The Anderson County Medical Society has elected the following officers for the coming year: Dr. Edward Dickson, Coal Creek, President; Dr. W. B. Barton, Briceville, Vice-President; Dr. J. S. Hall, Clinton, Secretary-Treasurer.

The Bedford County Medical Society has elected the following officers for the coming year: Dr. Alfred Farrar, Shelbyville, President; Dr. J. W. Reed, Belfast, Vice-President; Dr. W. H. Avery, Shelbyville, Secretary-Treasurer.

Dr. Alfred Blalock, Nashville, was a recent speaker at Duke University School of Medicine, Durham, North Carolina.

Deaths

Dr. Carroll Monroe Lovell, Dickson, aged 85, died November 17.

Dr. John Levi Roland, Obion, aged 49, died November 5 of injuries received when the automobile in which he was driving was struck by a train.

Dr. W. C. Officer, Monterey, aged 56, died December 25.

Dr. J. O. Nichols, Etowah, aged 65, died December 31 of pneumonia.

TEXAS

Dr. Guy F. Witt, Dallas, has been appointed a member of the Council of the Southern Medical Association from Texas for a regular Council term of five years, the appointment having been announced recently by the President, Dr. Fred M. Hodges, of Richmond. Dr. Witt succeeds Dr. Elbert Dunlap, of Dallas, who, having served the constitutional limit, was not eligible for reappointment.

The Baylor-Knox-Haskell Counties Medical Society has elected the following officers for the coming year: Dr. J. F. Bunkley, Seymour, President; Dr. T. W. Williams, Haskell, Vice-President; Dr. J. W. Foy, Seymour, Secretary.

The Bell County Medical Society has elected the following officers for the coming year: Dr. C. M. Simpson, Temple, President; Dr. J. W. Pittman, Belton, Vice-President; Dr. A. C. Scott, Jr., Secretary-Treasurer.

The Clay-Montague-Wise County Medical Society has elected the following officers for the coming year: Dr. L. C. Crook, Bellevue, President; Dr. E. W. Wright, Bowie, Vice-President; Dr. A. C. Irby, Bowie, Secretary-Treasurer.

The Coleman County Medical Society has elected the following officers for the coming year: Dr. J. M. Nichols, Coleman, President; Dr. R. H. Cochran, Coleman, Vice-President; Dr. M. E. Weaver, Coleman, Secretary.

The DeWitt County Medical Society has elected the following officers for the coming year: Dr. C. L. O'Quinn, Weesatche, President; Dr. F. A. Prather, Runge, Vice-President; Dr. James W. Eckhardt, Yorktown, Secretary-Treasurer.

The Eastland-Callahan Counties Medical Society has elected the following officers for the coming year: Dr. M. L. Stubblefield, Forman, President; Dr. T. G. Edwards, Cross Plains, Vice-President; Dr. J. H. Caton, Eastland, Secretary-Treasurer.

The Gray-Wheeler Counties Medical Society has elected the following officers for the coming year: Dr. G. R. Walker, Mobeetie, President; Dr. H. E. Nicholson, Wheeler, First Vice-President; Dr. C. B. Batson, McLean, Second Vice-President; Dr. C. D. Hunter, Pampa, Secretary-Treasurer.

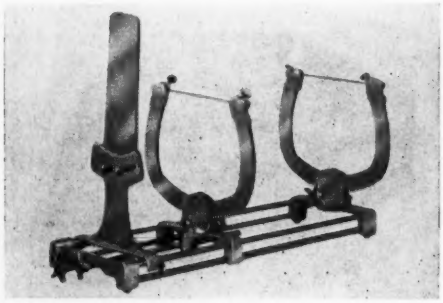
The Hidalgo-Starr County Medical Society has elected the following officers for the coming year: Dr. F. E. Osborn, McAllen, President; Dr. C. J. Martin, Rio Grande, Vice-President; Dr. J. B. Webb, Donna, Secretary-Treasurer.

The Hunt-Rockwell-Rains Counties Medical Society has elected the following officers for the coming year: Dr. Will Cantrell, Greenville, President; Dr. C. F. Neuville, Commerce, Vice-President; Dr. M. L. Wilbanks, Greenville, Secretary-Treasurer.

The Lubbock-Crosby County Medical Society has elected the following officers for the coming year: Dr. J. H. Stiles, Lubbock, President; Dr. E. L. Hunt, Lubbock, Vice-President; Dr. M. H. Benson, Lubbock, Secretary-Treasurer.

The Nolan-Fisher Counties Medical Society has elected the following officers for the coming year: Dr. E. W. Prothro, Sweetwater, President; Dr. C. U. Callan, Rotan, Vice-President; Dr. John Chapman, Sweetwater, Secretary-Treasurer.

Continued on page 36



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ASSISTANCE OFFERED TO MEDICAL WRITERS. Research, Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of the highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 413 St. James Place, Chicago, Ill.

ALCOHOLISM (30 years' experience)—THE STOKES HOSPITAL, 923 Cherokee Road, Louisville, Kentucky. Telephone, East 1488. Absolute privacy. Treatment one of gradual reduction. Do not limit the quantity of whiskey used in treatment. Each patient treated as an individual case. Craving for alcoholic beverages destroyed; no physical injury incurred. Rates and folder on request.

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WHEN massive edema occurs in the later stages of cardiac or cardio-renal disease, it adds materially to the burden of the heart. Unless the dropsical accumulations are quickly removed the chances of prolonging life are greatly reduced. As demonstrated by an abundance of clinical evidence, Salyrgan meets this important indication. Profuse diuresis usually sets in after three or four hours, and the quantity of fluid eliminated is often enormous. Amounts of 3 or 4 quarts are common and from 8 to 15 quarts may be observed.

Owing to the thoroughness with which Salyrgan acts, reaccumulation of fluid may be so controlled that it does not again assume serious proportions, and by occasional administration many patients have been kept comfortable for long periods.

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457M

Continued from page 34

The Potter County Medical Society has elected the following officers for the coming year: Dr. George Cultra, Amarillo, President; Dr. F. P. Miller, Amarillo, Vice-President; Dr. J. B. White, Amarillo, Secretary-Treasurer.

The Tarrant County Medical Society has elected the following officers for the coming year: Dr. Harold L. Warwick, Fort Worth, President-Elect; Dr. R. G. Baker, Fort Worth, Vice-President; Dr. Craig Hunter, Fort Worth, Secretary-Treasurer.

The Tom Green-Eight Counties Medical Society has elected the following officers for the coming year: Dr. W. D. Anderson, San Angelo, President; Dr. F. T. McIntire San Angelo, Vice-President; Dr. W. L. Bush, San Angelo, Secretary; Dr. J. B. McKnight, Sanatorium, Treasurer.

The Webb-Zapata-Jim Hogg Counties Medical Society has elected the following officers for the coming year: Dr. S. H. Graham, Laredo, President; Dr. V. L. Puig, Jr., Laredo, Vice-President; Dr. W. R. Powell, Laredo, Secretary-Treasurer.

The Wilbarger County Medical Society has elected the following officers for the coming year: Dr. W. C. Coleman, Vernon, President; Dr. B. D. Flaniken, Vernon, Vice-President; Dr. A. L. Borchardt, Vernon, Secretary-Treasurer.

The Bethania Hospital, Wichita Falls, recently elected the following officers: Dr. J. A. Heyman, Chief of Staff; Dr. J. E. Kanaster, Vice-President; Dr. R. L. Hargrave, Secretary.

The Memorial Hospital, Houston, has elected the following officers: Dr. A. T. Talley, President of the Staff; Dr. C. M. Warner, Vice-President; Dr. J. C. Youngblood, Secretary.

The Texas Radiological Society held its mid-winter meeting in Galveston January 18.

Dr. E. W. Griffey, Houston, has opened offices in the Medical Arts Building.

Dr. Fred A. Bloom, Houston, has moved to the Medical Arts Building.

Dr. Robert L. Currie, Houston, has moved to the Medical Arts Building.

Dr. Wilmer Adams has moved from Marfa to Shafter.

Dr. A. B. Currie has moved from Rocksprings to Junction.

Dr. Boyd C. Edwards has moved from Dodsonville to Union, Mississippi.

Dr. Conrad Frey has moved from Mason to Lockney.

Dr. R. H. Graham has moved from Wichita Falls to Clayton, New Mexico.

Dr. M. W. Harrison has moved from Conroe to Anahuac.

Dr. Harold W. Mann has moved from Gladewater to Rodessa, Louisiana.

Dr. John A. March has moved from Henrietta to Richards.

Dr. Dan W. Scott has moved from Freeport to Houston.

Dr. R. E. Selders has moved from Houston to Philadelphia, Pennsylvania.

Dr. C. G. Swift, Jr., has moved from Waco to Cameron.

Dr. Harold M. Block, Dallas, and Miss Jane Landau were married January 3.

Deaths

Dr. Cyrus Burford Weller, Austin, aged 54, died recently of chronic myocarditis.

Dr. Jesse Harper Lander, Victoria, aged 51, died recently.

Dr. Joshua Melvin Blackwell, Voth, aged 66, died in December of pneumonia.

Dr. John Morgan Johnson, Loving, aged 66, died November 24 of chronic myocarditis and bronchial asthma.

Dr. Charles A. Grimes, Bastrop, aged 67, died November 7 of cerebral hemorrhage.

Dr. Benjamin F. Crabtree, Dallas, aged 62, died December 3.

Dr. James David Stalsby, Crosby, aged 64, died recently.

Dr. Charles David Steinwinder, San Antonio, aged 45, died November 25 of uremia, acute nephritis and intestinal obstruction.

Dr. Frederick John Combs, San Antonio, aged 68, died November 26 of pyonephrosis and chronic nephritis.

Dr. Walter Israel Ducie, Galveston, aged 76, died November 29 of arteriosclerosis and chronic nephritis.

Dr. William Edward Campbell, Ennis, aged 58, died November 16 of chronic myocarditis.

Dr. James William DuVal, Wichita Falls, aged 67, died recently of coronary heart disease.

Dr. Harry Bergman, Livingston, aged 61, died November 20 of heart disease.

Continued on page 38

Direct Ovarian Therapy

A biologically assayed preparation of the ovarian follicular hormone. Stimulates the growth of the uterine muscle as well as the development of the vascularized hypertrophied endometrium necessary for the menstrual flow. For intensive treatment of amenorrhea, certain types of dysmenorrhea and the menopause.

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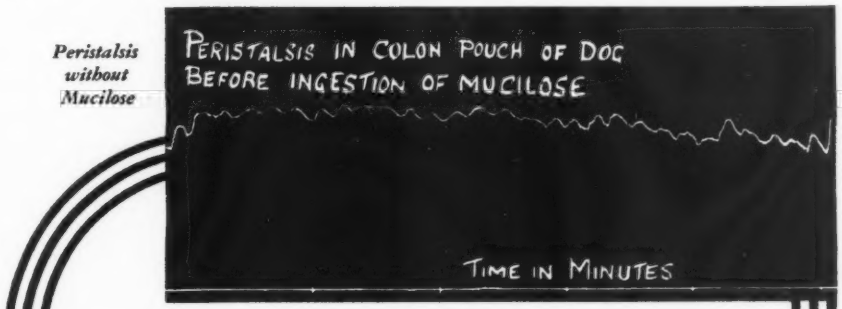

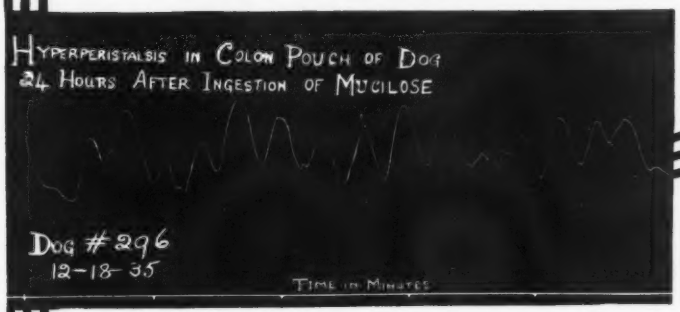

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1. supplies bland, *non-irritating distention*
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Please send me a supply of Mucilose for clinical test.

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Continued from page 36

Dr. James C. White, Paris, aged 80, died December 2 of acute indigestion.

Dr. D. L. Peeples, Navasota, aged 72, died November 28 of coronary occlusion.

Dr. Dana Elbra Monroe, Cameron, aged 51, died November 25.

VIRGINIA

The Accomac County Medical Society has elected the following officers for the coming year: Dr. Alva Mathews, Oak Hall, President; Dr. John W. Robertson, Onancock, Vice-President and Secretary-Treasurer.

The Floyd County Medical Society has elected the following officers for the coming year: Dr. S. T. Yeatts, Floyd, President; Dr. F. Clyde Bedsaul, Floyd, Secretary-Treasurer.

The Northampton County Medical Society has elected the following officers for the coming year: Dr. J. M. Lynch, Cape Charles, President; Dr. Griffin W. Holland, Eastville, Vice-President; Dr. W. Carey Henderson, Nassawadox, Secretary-Treasurer.

The Richmond Academy of Medicine has elected the following officers for the coming year: Dr. Roshier W. Miller, President; Dr. Emory Hill, First Vice-President; Dr. L. J. Stoneburner, Second Vice-President; Dr. Charles M. Caravati, Secretary.

Dr. B. H. Martin, Richmond, was recently appointed to membership on the Board of Supervisors of Henrico County.

Dr. Lee S. Liggan, Irvington, has been made Chaplain of the Odd Fellows Lodge of that city.

Dr. T. Latane Driscoll, Richmond, was recently made Honorary Grand Vice-President of the International Medical Fraternity, Alpha Kappa Kappa.

Dr. William Reese, Petersburg, has been made Vice-President of the Kiwanis Club of that city.

Dr. Herbert C. Jones, Petersburg, has been made First Vice-President of the Petersburg Chamber of Commerce.

Dr. Q. H. Barney has been made Health Officer of Alta Vista, succeeding the late Dr. J. Arnold Board.

Dr. R. L. Hudnall, Beverlyville, has been made a member of the Board of Supervisors of Northumberland County.

Dr. B. J. Atkinson, North Emporia, was recently made Chairman of the Public Health Committee of the Emporia Chamber of Commerce.

Dr. Francis H. McGovern, Danville, announces his association with Dr. M. H. Watson in the practice of diseases of the eye, ear, nose and throat.

Dr. Robert H. Detwiler, formerly of Washington, D. C., has located in Clarendon.

Dr. S. A. Draper, formerly of Christiansburg, has located in Roanoke.

Dr. J. E. Gladstone, formerly of Exmore, has located at Elkton.

Dr. F. T. Hauser, formerly of Bland, has located at Fortress Monroe.

Dr. James W. Hunter, Norfolk, has moved to the Medical Arts Building.

Dr. John Glen McNiel, Pennington Gap, and Miss Mary Roberts Kuyk were married December 28.

Dr. Charles Walton Purcell, University, and Miss Cleo Virginia Ashby were married in January.

Dr. Paul D. Camp, Richmond, and Miss Nellie Cornelia Staves were married on December 7.

Dr. Leland Floyd Hobbs, Jewell Ridge, and Miss Catherine Jones were married November 30.

DEATHS

Dr. William Elmer Ritter, West Graham, aged 72, died recently of cerebral hemorrhage.

Dr. Walker Ayett Campbell, Old Church, aged 60, died January 21.

Dr. Charles W. Gleaves, Wytheville, aged 80, died December 12.

Dr. George W. Richardson, West Point, aged 76, died December 29 from a stroke of apoplexy.

Dr. Francis Vaughan Fowlkes, Richmond, aged 69, died January 20.

WEST VIRGINIA

The Eastern Panhandle Medical Society elected the following officers for the coming year: Dr. Halvard Wanger, Shepherdstown, President; Dr. E. H. Bitner, Martinsburg, First Vice-President; Dr. A. B. Eagle, Martinsburg, Second Vice-President; Dr. Edwin Cameron, Martinsburg, Secretary-Treasurer.

The Fayette County Medical Society has elected the following officers for the coming year: Dr. P. E. Prillaman, Oak Hill, President; Dr. G. G. Hodges, Kilsythe, First Vice-President; Dr. W. E. Bundy, Minden, Second Vice-President; Dr. W. D. Simmons, Glen Ferris, Secretary-Treasurer.

The Hancock County Medical Society has elected the following officers for the coming year: Dr. J. E. Richmond, Weirton, President; Dr. L. A. Whitaker, Weirton, Secretary-Treasurer.

The Lewis County Medical Society has elected the following officers for the coming year: Dr. Ralph M. Fisher, Weston, President; Dr. Robert White, Hurst, Vice-President; Dr. Theresa O. Snaith, Weston, Secretary-Treasurer.

The Marshall County Medical Society has elected the following officers for the coming year: Dr. H. B. Ashworth, Moundsville, President; Dr. H. S. Parker, McMechen, Vice-President; Dr. J. A. Striebich Moundsville, Secretary-Treasurer.

The Raleigh County Medical Society has elected the following officers for the coming year: Dr. W. W. Hume, Beckley, President; Dr. S. A. Ford, Edwight, and Dr. R. P. Daniel, Pemberton, Vice-Presidents; Dr. L. M. Halloran, Beckley, Secretary-Treasurer.

The Tyler-Wetzel County Medical Society has elected the following officers for the coming year: Dr. John O. Theiss, New Martinsville, President; Dr. Gene M. Harsha, Sistersville, Vice-President; Dr. L. P. Stanley, Pine Grove, Secretary.

The Marion County Medical Society had as guest speaker at a recent meeting Dr. William F. Rienhoff, Baltimore, Maryland.

DEATHS

Dr. Robert M. McMillen, Wheeling, aged 73, died November 29 of cerebral edema.

Dr. Ernest Jacob Wichterman, Masontown, aged 52, died December 20 of cerebral hemorrhage.

Dr. Bernard Pogue Garred, Charleston, aged 80, died January 19.

Dr. John R. Boyd, Oakvale, aged 70, died January 20 of a heart attack.

Dr. John W. Bosworth, Philippi, aged 99, died January 3.

Dr. Alexander Irvine, McDowell, aged 73, died January 14 from a heart attack.

Dr. William B. Richardson, Parkersburg, aged 45, died January 1 of coronary occlusion.

Dr. Daniel C. Louchery, Clarksburg, aged 80, died January 3.

Doctor, Try This Golden Elixir

ELIXIR BROMAURATE

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excellent therapeutic results in

Whooping Cough

● ELIXIR BROMAURATE cuts short the duration of the illness, reduces the frequency of the attacks, relieves the distressing cough and gives the child rest and sleep.

● ELIXIR BROMAURATE is prescribed routinely by experienced physicians in all COUGH DISORDERS. Also valuable in the cough of PULMONARY TUBERCULOSIS and in BRONCHITIS and BRONCHIAL ASTHMA. Neurologists are using the Elixir with good effect in CHOREA, MIGRAINE and PETIT-MAL.

● ELIXIR BROMAURATE is a standard, assayed and palatable preparation. In four-ounce original bottles; the dosage is a teaspoonful 3 to 4 times a day after meals or more often when necessary.

NOTE—An interesting booklet on "Gold in the Treatment of Whooping Cough and Other Diseases" is just off the press and may be had on request. Drop us a card.

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Authorities Suggest a 25 AMPUL COURSE

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FOR ARTHRITIS THERAPY

The suggested course of arthritis therapy with Sulisocol requires 25 Hyposols (ampuls), of 2 cc (20 Mgms) each for maximum results.

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By planning sulphur treatments on this basis, you will assure satisfactory results. Most important—Use a product of known concentration and established activity.

Hyposols Sulisocol is the only colloidal sulphur in sterile aqueous clear autoisotonized solution with characteristic color of sulphur. It is the only one which may be safely used either intravenously or intramuscularly and is rarely followed by pain or reactions. Sulisocol is supplied in Hyposols (ampuls) of 1 cc, containing 10 Mgms., and 2 cc, containing 20 Mgms., packaged in boxes of 25 Hyposols.

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In the relief of gastric hyperacidity, *speed* is essential—Cal-Bis-Ma provides it. The neutralizing effect should be *prolonged* so as to prevent secondary acid rise—again Cal-Bis-Ma takes care of that. The irritated gastric mucosa should be soothed and protected from further irritation—that, too, is an important mission of Cal-Bis-Ma. Send for a trial supply and descriptive literature.

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Cal-Bis-Ma (powder) is supplied in tins (with removable label) containing 1¾ and 4 ounces and one pound. *Tablets*, in bottles of 110.

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The Story of MEAD'S OLEUM PERCOMORPHUM

A NEW, ECONOMICAL, POTENT SOURCE OF NATURAL VITAMINS A AND D

OLEUM PERCOMORPHUM, or Percomorph Liver Oil, is the achievement of an intensive, 10-year investigation conducted in the research laboratories of Mead Johnson & Company to find a natural oil more potent in vitamins A and D than cod liver oil and less expensive to the patient.

The U. S. Pharmacopoeia (IX, 1916, and X, 1925) recognized cod liver oil as the oil from the livers of fishes of the family *Gadidae*. There being some 50 species in this family, in addition to the type species, *Gadus Morrhua*, our first studies were directed at the examination of the more important species classed as cod. It occurred to us that somewhere in nature there might exist a species, or a family, or an order of fish, the liver oil of which would make possible a mixture comparable with Oleum Morrhuae but higher in vitamin potency.

The study was then directed to other species. By 1927 we had quantitatively compared the antiricketic value of oils from 15 species of fish and 11 other oils and fats. This was the most extensive survey of vitamin D sources reported up to that time. Outstanding in this list was puffer fish liver oil with a vitamin potency 15 times that of cod liver oil. Puffer fish were not available in commercial amounts, but the fact that one species of fish yielded so high a vitamin store provided great stimulus to investigators.

We discovered that the potency of fish liver oils increases with the leanness of the livers. With this revelation, we began a survey of all available commercial fish, as well as of rarer species. Collectors were sent to distant continents and to the islands of the Pacific and Atlantic oceans. From ports which never before knew cold storage we arranged to obtain refrigerated livers for our experiments. This ichthyological survey was interrupted (1928) at the time we introduced activated ergosterol.

In 1929 the Norwegian investigator, Schmidt-Nielsen, reported halibut liver oil to be superior to cod in vitamin A. Upon investigating, we felt then, as we do now, that while halibut liver oil marked a distinct advance it left much to be desired since it was perforce an expensive source of vitamin D. Hence it came to be used chiefly to supply vitamin A as a vehicle for viosterol.

Continuing the search for fish liver oils, by 1934 our laboratory staff had made thousands of bioassays of oils from more than 100 species to determine their vitamin characteristics. The results, reported in scientific journals in January and April 1935, were the culmination of a search literally of the seven seas.

With cumulative data on more than 100 species, it became evident that the fish belonging to the order known as *Percomorphi* differ from others in possessing, almost without exception, phenomenal concentrations of vitamins A and D. Thus we find liver oils which contain 50, 100, 500, and even 1,000 times as much vitamin A or vitamin D as average cod liver oil!

Percomorph liver oils are seldom equally rich in both vitamins. By skilful blending of the A-rich oils with the D-rich oils, a mixture is obtained which is about 200 times richer than cod liver oil in both vitamins A and D. As this concentration is so great that an ordinary dose of the oil could not be conveniently measured, we dilute the percomorph oil with approximately one volume of refined cod liver oil.

The resultant product is Mead's Oleum Percomorphum, 50%, which is 100 times cod liver oil* in both vitamins A and D. By a further dilution we obtain Mead's Cod Liver Oil Fortified With Percomorph Liver Oil, 10 times as potent as cod liver oil* in both vitamins A and D. Their respective potencies are 60,000 vitamin A units, 8,500 vitamin D units; and 6,000 vitamin A units, 850 vitamin D units (U.S.P.) per gram.

Just as Oleum Morrhuae is a mixture of the liver oils of various cod species (cf. U.S.P. XI, 1935, p. 261) so Mead's Oleum Percomorphum is a mixture of the liver oils of various percomorph species.** The significant difference is that the improved product is 100 times as potent* in both vitamins A and D.

Mead's Oleum Percomorphum, 50%, is available in 10-drop capsules, 25 in a box; and in 10 cc. and 50 cc. bottles. Mead's Cod Liver Oil Fortified With Percomorph Liver Oil is available in 3 oz. and 16 oz. bottles.

*U.S.P. XI Minimum Standard.
**Principally *Xiphias gladius*, *Pneumatophorus diego*, *Thunnus thynnus*, *Stereolepis gigas*, and closely allied species.

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Pediatric Acceptance of DEXTRI-MALTOSE is Constantly Increasing

Continued down from 1911

1934

"The question of carbohydrate is one of individual tolerance. Personally, I like Dextri-Maltose."—*L. Fischer: Pediatric progress during the last fifty years, Arch. Pediat. 51:207-218, April 1934.*

1934

"Cow's milk has a caloric value of 20 calories per ounce. Dextri-Maltose, commonly used, has 120 calories per ounce. As an example let us say that we have a well baby four months of age weighing 14 pounds. According to the rule, he should have 45 calories per pound per day, or 630 calories. Sugar requirements will be 1½ ounces—that is, 180 calories. Then deduct this from the 630 calories needed for the day and this leaves 450 calories to be supplied from the milk. 450 divided by 20 calories makes 22½ ounces of milk needed. The baby will probably take 7 ounces at each feeding and five feedings will be needed or a total of 35 ounces. This will leave 12½ ounces of water to be added and your formula will be:—

22½ ounces of cow's milk
12½ ounces of water
1½ ounces of Dextri-Maltose

Divide into five feedings of 7 ounces each and feed every four hours."—*B. F. Thomas: Infant care and feeding, J. M. A. Alabama 3:348-351, April 1934.*

1934

"Within a week it became necessary to place the baby entirely on a milk formulae. This was a mixture of milk, water, and dextri-maltose, and he thrived on it."—*J. M. Higgins: Acute lymphatic aleukemic leukemia, Pennsylvania M. J. 37:818-819, July 1934.*

1934

"The dietetic treatment of pylorospasm yields gratifying results, the use of a thick farina formula usually proving successful. This is prepared as follows:

Skimmed milk	10 ounces
Water	12 ounces
Farina	5 level tablespoonfuls
Dextri-maltose No. 1	3 level tablespoonfuls

"Mix the milk and water together and bring to a boil. Then sprinkle in slowly 5 level tablespoonfuls of farina and boil over a direct flame for five minutes, stirring continually. Transfer to a double boiler and cook for one hour. After the mixture is cooked add the dextri-maltose."—*C. S. Raue: The dietetic treatment of nutritional disorders in infancy, Hahneman. Monthly 69:522-528, July 1934.*

1934

"The mother's breast feedings were complemented by a mixture of three quarters milk, water and dextrimaltose. After a loss of 5 ounces (175.1 Gm.) during the first three days, the child gained steadily, weighing 7 pounds and 5 ounces (3,316.9 Gm.) by the eighth day."—*S. S. Brown, M. Morrison and D. A. Meyer: Anemia of the new-born without erythroblastosis: Observations at autopsy, Am. J. Dis. Child. 48:335-345, Aug. 1934.*

1934

For pyloric stenosis, "He was given atropine sulphate grains 1/1000 before each feeding and this was increased to grains 1/500 before vomiting was controlled. The formula consisted of cow's milk 16 ounces, water 16 ounces, dextri-maltose 2 level tablespoonfuls and uncooked farina 6 tablespoonfuls. He was fed 6 tablespoonfuls every 4 hours, 6 feedings a day . . . . In 5 days time there was a gain of 25 ounces. He was under treatment for a period of 5 months and 26 days during which time there was a gain of 14 pounds and 7 ounces."—*R. D. Hostetter: Pyloric stenosis, Ohio State M. J. 30:505-508, Aug. 1934.*

1934

"A formula of cow's milk, water, and dextri-maltose was given. The feedings were well taken, and the stools were normal."—*J. L. Rothstein: Low calcium tetany in the newborn, J. Pediat. 5:341-351, Sept. 1934.*

1934

"Meads Dextri Maltose is preferred, as it is not advertised to the laity. It contains dextrins and maltose in almost equal amounts, and in the three varieties varies only in the amount of sodium chloride and potassium bicarbonate they carry."—*G. Wiswell: Proprietary foods in infant feeding, Nova Scotia M. Bull. 13:483-485, Oct. 1934.*

1934

"Dextri-Maltose is, of course, the best sugar but expensive.* Cane sugar gives fairly satisfactory results except in very advanced cases, when dextrimaltose must be given."—*K. C. Chaudhuri: Marasmus and its treatment, M. Digest 2:246-249, Oct. 1934.*

1934

"To be sure, one can still raise well infants, using commercial granulated sugar, but one has a distinctly safer feeling, in the presence of disease, when a combination of sugars, such as dextrins and maltose, can be employed."—*L. C. Schroeder: The treatment of pneumonia in infants and children, M. Clin. North America 18:811-826, Nov. 1934.*

1934

In pyloric stenosis, "Finally, if the stools are incline l to be hard and dry and the fluid intake falls below 2.5 to 3 oz. per pound body-weight, additional fluids, preferably in the form of a solution of one of the dextrin-maltose preparations, between feedings, will usually be sufficient."—*C. C. Fischer: Constipation in infancy and childhood, Hahneman. Monthly 69:913-918, Dec. 1934.*

1934

"A sugar of the dextri-maltose type seems to be the most consistently and universally satisfactory."—*H. D. Lynch: Fundamentals of infant feeding, J. Indiana M. A. 27:571-574, Dec. 1934.*

1934

"In pyloric stenosis in infants it is usually held that immediate operation is indicated, but Sauer believes that thick cereal feedings should be tried for a time to see if improvement will not take place; . . . The mixture used is skimmed milk, 9 ounces; water, 12 ounces; farina or rice flour, 6 teaspoonfuls; dextrimaltose, 3 ounces; boil an hour or more in a covered double boiler until thick. . . . This non-operative treatment was effective in 28 of his 35 cases."—*H. Beckman: Treatment in General Practice, ed. 2, W. B. Saunders Co., Phila., 1934, pp. 408, 409.*

1934

"Mixtures of maltose and dextrins ferment less readily in the intestines."

"Preparations of dextri-maltose are said to be less fermentable than cane sugar or milk sugar, and it is the custom to add one of these in the treatment of diarrhoea."—*H. P. Wright: Essentials of Infant Feeding and Paediatric Practice, Oxford University Press, London, 1934, pp. 31, 95.*

1934

In diarrhea, "Sugar, preferably one of the dextrin-maltose preparations, is added in gradually increasing doses until finally a return to an ordinary cow's milk mixture is made."

"Sugar, which is less well tolerated than protein, may be added in small quantities to the feeds at the end of thirty-six or forty-eight hours, and some preparation of maltose will be found better than cane sugar, lactose or glucose."—*R. Hill: The treatment of diarrhoea in infants, in C. P. G. Wakeley: Modern Treatment in General Practice, William Wood & Co., Baltimore, 1934, pp. 220, 221.*

(to be continued)

When More Physicians Specify MEAD'S, More Babies Will Be Fed By Medical Men

***It is interesting to note that a fair average of the length of time that an infant receives Dextri-Maltose is five months: That these five months are the most critical of the baby's life: That the difference in cost to the mother between Dextri-Maltose and the very cheapest carbohydrate at most is only $6 for this entire period—a few cents a day: That, in the end, it costs the mother less to employ regular medical attendance for her baby than to attempt to do her own feeding, which in numerous cases leads to a seriously sick baby eventually requiring the most costly medical attendance.**

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MENINGOCOCCUS ANTITOXIN

DEVELOPED IN THE RESEARCH LABORATORIES OF PARKE, DAVIS & COMPANY

"Meningococcus Antitoxin has reduced by approximately 50 per cent the deaths from meningococcic meningitis at Cook County Hospital."

Journal of the American Medical Association, Volume 104, page 980, March 23, 1935.

THE introduction of Meningococcus Antitoxin is a significant contribution to the therapy of contagious diseases. Extensive biological and clinical research has led to the development of this true antitoxin, markedly effective in lowering the mortality in meningococcic meningitis.

Accepted for inclusion in New and Nonofficial Remedies by the Council on Pharmacy and Chemistry of the American Medical Association.

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